JULY, 1950

The Review of Gastroenterology

OFFICIAL PUBLICATION

NATIONAL GASTROENTEROLOGICAL ASSOCIATION

The Present Status of the Treatment of Cirrhosis of the Liver

Surgical Aspects of Diverticulitis of the Sigmoid

The Antibiotics in Gastrointestinal Diseases

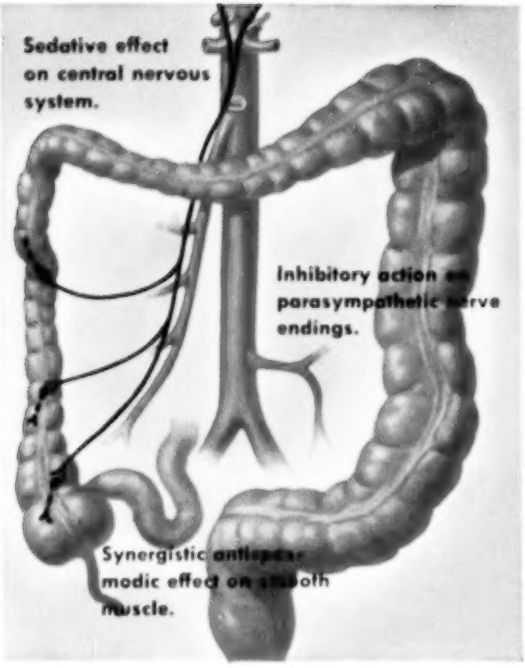
Thoughts Upon Diabetes Today

Recurrent Inguinal Hernia

●

Fifteenth Annual Convention
New York, N. Y., 9, 10, 11 October 1950

VOLUME 17 NUMBER 7


Sedative effect on central nervous system.
Inhibitory action on parasympathetic nerve endings.
Synergistic antispasmodic effect on smooth muscle.

Trasentine-Phenobarbital

An ideal antispasmodic for prolonged use

TRASENTINE-PHENOBARBITAL is singularly free of side effects such as dryness of the mouth, pupillary dilatation and palpitation of the heart. TRASENTINE has very little cumulative effect even in large doses over a long period of time, although it is a powerful antispasmodic. Thus TRASENTINE-PHENOBARBITAL is an ideal spasmolytic agent for patients who must be treated over many months.

Prolonged illness produces an anxiety state in many patients which may noticeably retard improvement. TRASENTINE-PHENOBARBITAL relieves psychic tension and speeds recovery of these patients.

Wide use is being made of TRASENTINE-PHENOBARBITAL in daily practice to relieve pain and spastic conditions of the abdominal viscera associated with hyper-excitability of the autonomic system.

One or two tablets may be given three or four times a day. If used over long periods of time, therapy should be interrupted periodically because of the phenobarbital content.

TRASENTINE-PHENOBARBITAL—Tablets (yellow) contain 50 mg. TRASENTINE hydrochloride with 20 mg. phenobarbital.

TRASENTINE—Tablets (white) of 75 mg.; Suppositories of 100 mg.; Ampuls of 50 mg.

Ciba PHARMACEUTICAL PRODUCTS, INC., SUMMIT, NEW JERSEY

TRASENTINE® (brand of adiphenine) 2/1[illegible]

The Neurogenic Approach–

in Peptic Ulcer Therapy

Banthine*

BROMIDE

Brand of Methantheline Bromide

PHARMACOLOGY

Unlike the antacid drugs, Banthine does not effect its action within the gastrointestinal canal, but on the nervous mechanism.

Laboratory and clinical observations indicate that it acts as a true anticholinergic drug. Its effects take place at both the parasympathetic and sympathetic ganglions, and at the parasympathetic postganglionic nerve endings.

THERAPEUTIC ACTION

As a result of reducing the vagotonia of ulcer patients, Banthine consistently decreases hypermotility and usually decreases hyperacidity.

Clinical experience has evidenced the rationale of this approach. Subjectively, ulcer symptoms have been relieved as soon as fifteen minutes after the first dose, with continued relief as long as the drug is continued at regular intervals. Objectively, motor and secretory inhibition has been demonstrated by intragastric balloon, analysis of gastric contents and other laboratory procedures; healing of resistant ulcers has been demonstrated roentgenographically.

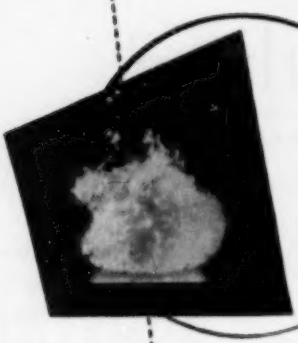
TOXICITY AND PRECAUTIONS

Symptoms, such as some dryness of the mouth, mild blurring of vision, slight difficulty of urination or gastric fulness, may occur but usually disappear or decrease on continued medication; if severe, they may require dosage readjustment. Untoward reactions with Banthine therapy have not been encountered after eighteen months of clinical use.

*Trademark of G. D. Searle & Co., Chicago 80, Illinois.

AVERAGE DOSAGE: *One or two tablets (50 or 100 mg.) every six hours around-the-clock.*

BANTHINE IS A PRODUCT OF SEARLE RESEARCH



Every physician should see this!

Drop a Syntrogel tablet in water. In a matter of seconds it will "fluff up" to several times its size—proof of instant disintegration—tremendous increase in adsorptive surface. This is why Syntrogel relieves "heartburn" and hyperacidity so quickly.

HOFFMANN-LA ROCHE INC • NUTLEY 10 • N. J.

Syntrogel®

Each Syntrogel tablet contains aluminum hydroxide, calcium carbonate, magnesium peroxide and Syntropan® 'Roche.'

'Roche'

The REVIEW *of* GASTROENTEROLOGY

(Incorporating the American Journal of Gastroenterology)

The Pioneer Journal of Gastroenterology, Proctology and Allied Subjects in the United States and Canada

Volume 17 JULY, 1950 Number 7

CONTENTS

Page

Editorial Board 528

General Information 530

The Present Status of the Treatment of Cirrhosis of the Liver
Chester S. Keefer, M.D. 533

Thoughts Upon Diabetes Today ..... *Elliott P. Joslin, M.D.* 545

The Antibiotics in Gastrointestinal Diseases ..... *Maxwell Finland, M.D. and E. Buist Wells, M.D.* 558

Recurrent Inguinal Hernia ..... *Roger T. Doyle, M.D.* 563

Acute Perforated Peptic Ulcer ..... *Charles G. Shedd, M.D., F.A.C.S. and I. Schwartz, M.D.* 568

Surgical Aspects of Diverticulitis of the Sigmoid..... *J. Edward Flynn, M.D., F.A.C.S.* 577

Diaphragmatic Hernia with Report of a Case.... *Roy Upham, M.D., F.A.C.S., F.I.C.S.* 586

Treatment of Giardiasis by the Chloroguanide Chlorhydrate
Albert Albornoz Plata, M.D. 598

Corticodiencephalic Gastrointestinal Syndromes in Epileptics (Part VII)
Thomas S. P. Fitch, M.D., F.A.C.S., Albert W. Pigott, M.D., B.S. and Samuel Weingrow, M.D. 602

Book Reviews 618

Owned and published monthly by the National Gastroenterological Association, Inc. Editorial Office: 146 Central Park West, New York 23, N. Y. Business Office: 1819 Broadway, New York 23, N. Y. Copyright, 1950, by the National Gastroenterological Association, Inc. Subscription rate, U. S., Pan-American Union: One year $5.00, two years $9.00 (foreign $7.00, $13.00) Single copy: $.50. *Reentered as second class matter, February 24, 1947, at the Post Office at New York, N. Y., under the act of March 3, 1879.*

Index to Advertisers

Ames Co., Inc. 532
Burton, Parsons & Co. 622
Ciba Pharmaceutical Products, Inc. ..... 2nd Cover
Coca-Cola Co. 617
Endo Products, Inc. 621
Hoffmann-LaRoche, Inc. 526
Massengill, S. E., Co. 624
Reynolds, R. J., Tobacco Co. 529
Sandoz Chemical Works, Inc. 611
Schenley Laboratories, Inc. 613
Searle, G. D., & Co. 523
Sharp & Dohme 535
U. S. Treasury 620
Warner, Wm. R. ..... 3rd Cover
Winthrop-Stearns, Inc. 619
Wyeth, Inc. ..... 4th Cover

The Review of Gastroenterology

OFFICIAL PUBLICATION

of the

NATIONAL GASTROENTEROLOGICAL ASSOCIATION

1819 Broadway, New York 23, N. Y.

Editorial Office, 146 Central Park West, New York 23, N. Y.

SAMUEL WEISS, *Editor*

EDITORIAL BOARD

ANTHONY BASSLER — HARRY M. EBERHARD

WILLIAM W. LERMANN

EDITORIAL COUNCIL

F. W. BANCROFT
W. A. BASTEDO
RICHARD BAUER
BENJAMIN M. BERNSTEIN
THEODORE BLUM
DONOVAN C. BROWNE
JOSE OVIEDO BUSTOS
JOHN CARROLL
LOUIS H. CLERF
F. J. CONLAN
FRANK A. CUMMINGS
FELIX CUNHA
RUDOLF R. EHRMANN
MAX EINHORN
HYMAN I. GOLDSTEIN
CHEVALIER L. JACKSON
WM. C. JACOBSON
I. R. JANKELSON
SIGURD W. JOHNSEN
ELIHU KATZ
RICHARD KOVACS
FRANZ J. LUST
G. RANDOLPH MANNING
CHARLES W. MCCLURE
GEORGE G. ORNSTEIN
GEORGE T. PACK
GEORGE E. PFAHLER
A. SUMNER PRICE
HENRY A. RAFSKY
MARTIN E. REHFUSS
DAVID J. SANDWEISS
JOSEPH SCHROFF
MARKS S. SHAINE
I. SNAPPER
HORACE W. SOPER
WILLIAM H. STEWART
J. E. THOMAS
MAX THOREK
C. J. TIDMARSH
GABRIEL TUCKER
CARLOS BONORINO UDAONDO
ROY UPHAM
F. H. VOSS
MICHAEL WEINGARTEN
LESTER R. WHITAKER
FRANK C. YEOMANS

ABSTRACT STAFF

ADOLPH ABRAHAM, *Chairman*

LESTER L. BOWER
A. J. BRENNER
JOHN E. COX
LEROY B. DUGGAN
RICHARD I. KILSTEIN
ARTHUR A. KIRCHNER
WILLIAM LIEBERMAN
LIONEL MARKS
LOUIS K. MORGANSTEIN
WILLIAM L. PALAZZO
JACOB A. RIESE
H. M. ROBINSON
A. X. ROSSIEN
MARKS S. SHAINE
A. SLANGER
REGINALD B. WEILER

Business Office, 1819 Broadway, New York 23, N. Y.

DANIEL WEISS, *Managing Editor*

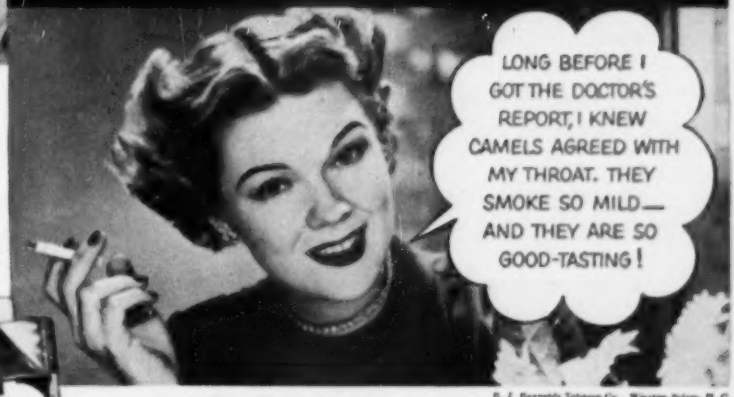
STEVEN K. HERLITZ, *Advertising Manager*

Throat Specialists report on 30-day test of Camel smokers:

"Not one single case of throat irritation due to smoking Camels!"

Yes, these were the findings of throat specialists after a total of 2,470 weekly examinations of the throats of hundreds of men and women who smoked Camels—and only Camels—for 30 consecutive days

Elaine Bassett, television stylist, is one of hundreds, coast to coast, who made the 30-Day Test of Camel Mildness under the observation of throat specialists.



R. J. Reynolds Tobacco Co., Winston-Salem, N. C.

ACCORDING TO A NATIONWIDE SURVEY:

More Doctors Smoke Camels

THAN ANY OTHER CIGARETTE

Yes, doctors smoke for pleasure, too! In a nationwide survey, three independent research organizations asked 113,597 doctors what cigarette they smoked. The brand named most was Camel.

GENERAL INFORMATION

Contributions: Articles are accepted for publication on condition that they are contributed solely to THE REVIEW OF GASTROENTEROLOGY.

Manuscripts should be typewritten double-spaced and the original copy submitted. Footnotes and bibliographies should conform to the style recommended by the American Medical Association.

Illustrations and diagrams should carry suitable lettering and explanations. Four illustrations per article are allowed without cost to the author.

News items of interest will receive due consideration.

REVIEWS: THE REVIEW OF GASTROENTEROLOGY will review monographs and books dealing with gastroenterology or allied subjects. It may be impossible to review all material sent. However, an acknowledgement will be made in the Department of Reviews.

The editors and publishers are not responsible for individual opinions expressed by their contributors, nor for those given under current literature.

Reprints: A price list and order blank for reprints will be sent to each contributor before the journal is issued.

Manuscripts, abstracts, books for review and news items are to be sent to the Editorial office, 146 Central Park West, New York 23, N. Y.

Communications regarding business matters, advertising, subscriptions and reprints should be sent to the Business office, 1819 Broadway, New York 23, N. Y.

Subscription price: U.S. and Pan-American Postal Union: one year, $5.00, two years, $9.00. Elsewhere, $7.00, $13.00. Single copy $.50. Members of the National Gastroenterological Association receive the REVIEW as part of their membership.

Change of Address: Notify publishers promptly of change of address. Notices should give both old and new addresses.

Cremothalidine is a smooth, exceptionally palatable suspension of *Sulfathalidine*® phthalylsulfathiazole, a remarkably effective, nontoxic enteric bacteriostat, only 5% of which is absorbed from the bowel. *Cremothalidine* is particularly acceptable to children, but is useful in all age groups. It is indicated especially for ulcerative colitis, *E. coli* infections of the urinary tract, and for enteric bacteriostasis in intra-abdominal surgery. *Cremothalidine* is supplied in convenient, wide-mouth *Spasaver*® bottles of 8 fluidounces.
Sharp & Dohme, Philadelphia 1, Pa.

SHARP & DOHME

Cremothalidine®

Sulfathalidine Suspension

Simplified dosage . . . superior Sulfonamide

practical ideals in diabetes

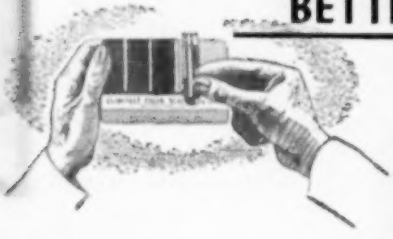
EARLY DIAGNOSIS

"The ideal detection center is in the private physician's office."[1] This approach to widespread early diagnosis of diabetes can be practical when *every routine examination of every patient includes urine-sugar analysis.* Routine analysis, in turn, is more practical for the physician who uses *Clinitest* (Brand) Reagent Tablets. The test is simple, rapid and self-contained (no external heating). Results are known at once

CLINITEST

REAGENT TABLETS ***for urine-sugar analysis***

BETTER CONTROL



"Generally, only the well controlled diabetic patient may expect to live to normal expectancy and without premature arterial degeneration."[2] Here too, practicality recommends *Clinitest.* The *Clinitest* (Brand) Urine-sugar Analysis Set (a compact pocket unit) enables the patient, under the physician's guidance, to make regular checkups simply, accurately and conveniently. This is a practical guarantee of the patient's cooperation without which adequate control by the doctor is hardly feasible.

Clinitest, reg. trademark

Bibliography: (1) Wilkerson, H. L. C.: New York State J. Med. 49:2045 (Dec. 15) 1949. (2) Sweeney, J. S.: Texas State J. Med. 45:623 (Sept.) 1949.

AMES COMPANY, INC · ELKHART, INDIANA
AMES COMPANY OF CANADA, LTD., TORONTO

The Review of Gastroenterology

(Incorporating the American Journal of Gastroenterology)

A monthly journal of Gastroenterology, Proctology and Allied Subjects

Volume 17 JULY, 1950 Number 7

THE PRESENT STATUS OF THE TREATMENT OF CIRRHOSIS OF THE LIVER*†

CHESTER S. KEEFER, M.D.

Boston, Mass.

During the past 15 years there has been a great improvement in the treatment of cirrhosis of the liver. Advances have been made possible by the numerous careful studies of disturbances in hepatic function that occur in patients with cirrhosis, and progress has been made in our understanding of the ways in which hepatic cells may be damaged. We know some of the general conditions in which liver damage occurs and we are familiar with some of the ways in which such damage may be prevented. Much less is known about the methods that will restore the damaged and malfunctioning liver cells to normal. However, in spite of our deficiencies in knowledge, it has been shown that improvement in the patient with hepatic cirrhosis follows the use of certain broad programs of treatment. They consist in the main of providing the patient with substances that stimulate growth of cells, supplying essential food materials that cannot be made by the malfunctioning liver, protecting the patient against infection, and providing agents that remove fat stores from the liver.

The general features of treatment are rest, discontinuing alcohol as a food and stimulant, supplying an adequate diet to maintain optimum nutrition, including adequate quantities of protein, carbohydrate, fat, accessory food substances such as Vitamin K, Vitamin A, Vitamin B-complex, ascorbic acid, liver extract, and dietary amino acid supplements, such as methionine and choline. Whole blood transfusions may be used for anemia, salt poor serum albumin for hypoproteinemia, and chemotherapy for infection.

In planning a program of treatment for patients with cirrhosis of the liver, it should be perfectly clear to both the patient and the physician that the disease is chronic with a tendency to relapse, and a program should be planned in terms of many months or several years, rather than weeks.

---

*Read before the Fourteenth Annual Convention of the National Gastroenterological Association, Boston, Mass., 24, 25, 26 October 1949.

†From the Department of Medicine, Boston University School of Medicine and the Evans Memorial, Massachusetts Memorial Hospitals, Boston, Massachusetts.

Before saying anything about the treatment of specific features of hepatic cirrhosis, I want to tell you something about the development of diffuse fibrosis of the liver.

The central lesion preceding diffuse fibrosis of the liver is fatty infiltration. One sees, not infrequently, patients with fatty infiltration of the liver before fibrosis of any considerable degree occurs. Fatty infiltration is encountered most often in patients who have used large amounts of alcohol[1] and have at the same time been on an inadequate diet. Also, it is encountered in areas of the world where the diet is greatly deficient in protein and in milk. This form of liver disease has shown improvement following the use of milk, protein, liver extract or powdered hog's stomach[2]. Fatty infiltration of the liver also is seen in patients with diabetes and in those with malnutrition accompanying chronic tuberculosis. In all of these conditions, diffuse hepatic fibrosis may develop when the patients survive the stages of marked fatty infiltration.

I want to stress the fact that fatty infiltration of the liver may cause hepatic insufficiency in the absence of fibrosis. Jaundice, ascites, edema, hemorrhagic phenomena and death which is sometimes sudden and quiet are all features of this form of liver disease. There seem to be good grounds then for believing that liver cells that are loaded with fat interfere with the circulation within the liver, with the excretion of bile pigment, and from the other clinical manifestations of hepatic insufficiency that are observed, there is good evidence that other vital functions of the liver are disturbed. Moreover, Conner[3] has shown that compression of liver cells at the periphery of the lobule by cells swollen with fat causes atrophy of the cells with resulting stimulation to fibrosis in the periportal areas. Rich and his associates[4] have pointed out that hepatic cells that are filled with fat have a regenerative activity that is far less than that of non-fatty cells in the same liver. Thus, the fatty liver is at a disadvantage when faced with a demand for regeneration. It is the belief of Rich that "the marked impairment of regenerative capacity in this fatty liver can play a significant role in the pathogenesis of cirrhosis that develops in the fatty liver, in that by inhibiting normal regenerative replacement of necrotic liver cells by new ones, the alternative occurrence of fibrosis is favored".

It would appear, therefore, that if diffuse hepatic fibrosis that follows fatty infiltration of the liver is to be prevented then the conditions under which it occurs must be recognized and proper measures taken. The first is the prevention of fatty infiltration of the liver. Secondly, in the presence of fatty infiltration, methods must be employed that are designed to remove the fat stores from the liver, and to stimulate the growth and regeneration of liver cells that are capable of regenerating.

Experimentally, fatty infiltration of the liver has been produced by a variety of methods, but chiefly by depriving an animal of "lipotropic factors" in the diet, and by the feeding of a high fat diet. The existence of "lipotropic" factors was demonstrated first by Best and McLean[5] when they were able to show that choline rapidly reduced an increased fat content of the liver to normal.

Fatty Infiltration of the Liver

In an attempt to correct defects in nutrition, remove fat from the liver, and to stimulate the growth of liver cells, various plans of "dietary" treatment have been employed. In the main, they have consisted of supplying the patient with a protein content that is adequate to maintain nitrogen equilibrium and protein products containing lipotropic factors are recommended—beef, casein, milk (whole), egg white. This is often supplemented with choline and methionine—two amino acids that are lipotropic. Carbohydrate is given for its energy producing factors and in an attempt to replace the fat in the liver with adequate amounts of glycogen. Fat is used in moderation to provide energy and to spare protein.

In view of the frequent association of the clinical features of vitamin deficiencies in cirrhosis of the liver, vitamin supplements have been recommended. These include Vitamin A, the B-complex, Vitamin C, tocopherol, Vitamin K.

Intramuscular and intravenous liver extract as well as large amounts of yeast have been recommended for their effect on liver cell growth. Whether or not these substances stimulate growth specifically is not known. However, good results have followed their use over a period of years when this treatment is combined with other forms of therapy.

A recent report by Ralli and her associates[6] suggests that patients with cirrhosis of the liver and ascites who received liver extract intravenously in their initial period of therapy have survived for a longer period than those who received liver extract intramuscularly. Moreover, it was the experience and observation of these students of the disease that the accumulation of ascitic fluid was controlled more effectively and this was associated with a more rapid increase in serum albumin.

Thus, it is seen that the evidence is good that diffuse fibrosis of the liver is preceded by fatty infiltration, and a considerable amount of information has accumulated that helps us in understanding some of the conditions that influence the infiltration of the liver with fat, and some of the conditions that withdraw fat from the liver.

The entire subject of nutritional factors in liver injury, both experimental and human, has been reviewed in an admirable manner by Himsworth in his monograph on "The Liver and Its Diseases"[7].

Treatment of Ascites and Edema

It is a well known clinical fact that patients with cirrhosis of the liver usually come under observation because they show jaundice or the signs that are interpreted as indicating portal venous hypertension. These latter signs include ascites, splenomegaly or hematemesis. There are, of course, many other signs that are present in some patients that suggest disordered hepatic function, or at least the features that are contributory to the development of the clinical picture of hepatic cirrhosis. I refer to the bleeding tendency, generalized edema, anemia, the signs of various deficiency disorders such as multiple neuritis, glossitis, fever and vascular phenomena.

With the development of new concepts concerning the pathogenesis of cirrhosis of the liver and with the introduction of types of treatment that are aimed at supplying deficiencies and promoting the regeneration of liver cells that can function properly, the length of life of patients with cirrhosis of the liver has been prolonged.

It should be stated at once that we do not know all of the factors that promote regeneration of liver cells following their damage or injury. We do know that such factors as an adequate blood supply to the liver, and the absence of biliary obstruction and infection are very important, also, the presence of normal cells that are capable of regeneration. Rich has demonstrated that cells that are filled with fat fail to regenerate, or at least they show very few mitotic figures.

First of all, I shall discuss the treatment of edema and ascites. They cannot be separated in any discussion because in some patients edema is outstanding and ascites is minimal. In others, ascites is present with little or no edema. It is now clear that the ascites associated with cirrhosis of the liver is due to a complex mechanism, and many factors play a part. These include a decrease of venous blood flow through the liver, a decrease in the oncotic pressure of the blood plasma due to a decrease in the circulating serum albumin, a retention of sodium and water that would appear to depend in part, at least, on the presence of an increased amount of a circulating antidiuretic hormone.

All of the observations that have been made in patients with cirrhosis of the liver show that the blood flow through the liver tends to be decreased below the average normal level. The degree of reduced blood flow varies tremendously with the stage of the disease, the degree of cirrhosis and the methods that are employed in such investigations. In some patients the evidence seems good that the decrease in hepatic blood flow is not very great, in a few the blood flow is normal and in some it is higher than normal. In most cases there is an increased arterial-venous oxygen difference.

The lowered oncotic pressure of the blood plasma resulting from the decreased plasma proteins plays an important part in the development of both ascites and edema. My interest in this subject was aroused some twenty years ago when I observed patients with latent cirrhosis of the liver who developed transitory ascites during an attack of bacillary dysentery associated with hypoproteinemia. When the patients recovered from their dysentery, the plasma proteins returned to normal and the ascites disappeared. It seemed reasonably clear, therefore, that the hypoproteinemia contributed to the development of ascites in these cases. Several years later Myers and I[8] studied a group of patients with cirrhosis of the liver, edema and ascites. From these studies it was plain that the presence of edema and ascites in many patients with cirrhosis of the liver could be correlated in part with the presence of hypoproteinemia. It became apparent, however, from the study of patients with acute liver disease that many of them retained water and sodium that were independent of hypoproteinemia. Moreover, when hepatic function improved, there was a spontaneous diuresis that was independent of plasma protein levels.

Inasmuch as many patients with cirrhosis of the liver and ascites had hypoproteinemia, it was only natural for us to explore the possibility of the causes for the decreased plasma proteins. It was concluded from the study of patients that multiple factors were concerned. First, these patients were unable to build their own plasma proteins in sufficient quantity to maintain a normal serum albumin; secondly, protein was being lost in the ascitic fluid, and those patients who were being tapped repeatedly lost large amounts of protein in this way.

Salt Free Albumin

When salt free serum albumin became available, it was possible to test the role of hypoalbuminuria in the production of ascites and edema, since by injecting adequate amounts of salt free serum albumin intravenously, the plasma albumin can be increased to the normal level and the results observed. All of the studies that have been made so far, including those of our own clinic, indicate that the formation or the decrease in ascites and edema is only partially influenced by the administration of salt free albumin. There are now available a number of very carefully studied cases of cirrhosis of the liver in which salt free serum albumin has been administered intravenously[9].

There is general agreement that following the intravenous injection of serum albumin there is an increase in colloid osmotic pressure of plasma to normal values, an increase in albumin concentration, and the colloid osmotic pressure of ascitic fluid, an increase in plasma volume, an increase in glomerular filtration rate and in renal plasma flow and an increase in urinary chloride excretion at the time of transitory diuresis. One feature of considerable importance is the fact that following the injection of serum albumin and the increase in plasma volume, there is an increased diffusion of albumin into the ascitic fluid. An increase in plasma volume is accompanied by an increase in portal pressure, and an increase in the diffusion of protein through the capillary walls.

The intravenous injection of salt free albumin may cause only a transitory diuresis, so that it may have very little effect on ascites and edema unless it is given over a long period of time, and unless the total plasma albumin is kept at a normal level. In some patients it has been possible to delay the recurrence of ascites by intravenous injection of serum albumin and this has been true in spite of the fact that it has been impossible to control the edema.

It would appear that serum albumin can play an important part in relieving patients of their symptoms, and it may carry them along until the liver has regenerated sufficiently to manufacture its own plasma proteins.

There are other important factors causing water retention when ascites and edema are present. They are increased intraabdominal pressure, delayed water absorption, and delayed water diuresis. Ascites causes increased intraabdominal pressure. When this is extreme the blood flow through the kidney and through the vena cava from the legs is decreased. The result is an increased edema of the legs and a decreased output of urine.

Thorington and Schmidt in 1923[10] pointed out that an increase of intraabdominal pressure to 30 mm. of mercury in dogs was uniformly followed by complete suppression of urine. When the pressure was less than 15 mm. of mercury there were no constant effects. Between 15 and 30 mm. of pressure there was a progressive diminution in the rate of urine excretion. They concluded that the suppression of urine with high intraabdominal pressure is probably due to a rise in abdominal venous pressure and that the effects on the renal circulation are comparable to those of partial occlusion of the renal veins.

Bradley and Halperin[11] have demonstrated in our own clinic at the Massachusetts Memorial Hospitals that increase in intraabdominal pressure in man causes a reduction of renal blood flow, and a cessation of urine formation in a certain proportion of nephrons.

Another effect of portal congestion has been shown by McMichael and Smivk[12], namely, a delay in the elimination of water by the kidneys. Following the experimental production of portal congestion in animals, there is a diminished absorption of water and a delay in diuresis. When venous anastomosis opens up, the delay in water absorption rate improves but it does not return to normal. The diuresis curve may return to normal, despite a moderate delay in water absorption.

It would appear, therefore, that portal congestion causes (1) delayed absorption of water from the gastrointestinal tract; (2) the increased intraabdominal pressure, if it is sufficiently high, will contribute to edema formation by increasing the venous pressure in the inferior vena cava and renal veins by virtue of the fact that there is a decreased urine excretion and slowing of blood flow through the legs.

That these factors play a part in water retention and edema in patients with cirrhosis of the liver and ascites is clearly shown by the fact that a number of patients have a prompt diuresis following abdominal tapping. When one studies the plasma proteins following paracentesis it is found that the total proteins frequently decrease during the first 12 to 24 hours after abdominal tapping and at a time when the urinary output increases. Thus it would appear that the diuresis that follows paracentesis may result from an increased absorption of fluid into the blood due to the decreased venous pressure in the lower extremities and an increase in the blood flow through the kidney.

Antidiuretic Hormones and Edema in Cirrhosis of the Liver

It is a matter of common experience to observe patients with acute hepatitis who develop edema without ascites during the course of their illness, or edema may appear long before the appearance of ascites[13,14]. Moreover, it is a well known clinical observation that edema may occur in these patients without a decrease in plasma proteins. Finally, improvement in the patients' general condition is often indicated by a spontaneous diuresis.

The explanation for the retention of sodium and water in patients with liver disease remains obscure. Ralli and her associates[14] have found an increased amount

of antidiuretic substances in the urine, and they suggest that these substances may contribute to the retention of water and sodium.

In any event, oliguria or at least a failure of the kidney to excrete sodium and water in normal amounts often leads to edema without a decrease in plasma proteins. The mechanism for this phenomenon remains obscure, but it is one of the most important problems requiring solution at present.

It would appear then that edema and ascites in patients with cirrhosis of the liver are dependent upon at least three factors: (1) the degree of portal hypertension; (2) the level of the oncotic pressure in the blood; (3) the function of the kidney insofar as the excretion of sodium chloride is concerned. The portal hypertension is dependent upon the amount of liver damage, i.e., either swelling of the liver cells as in fatty infiltration or fibrosis in the portal areas, and the total plasma volume. The level of the oncotic pressure in the blood is dependent upon the amount of circulating plasma albumin. This is determined in large part by the inability of the organism to synthesize plasma albumin in a normal fashion and the loss of protein in the ascitic fluid.

The reasons for the inability of the kidney to excrete sodium and chloride are obscure but it may be due in part to a homeostatic mechanism that tends to conserve salt in the face of the increased permeability of fluid into the tissues that accompanies the hypoproteinemia. That hypoproteinemia will not explain all of the phenomena that are observed in these patients is reasonably clear, since Faloon, Eikhardt, Cooper and Davidson[9b,c,d] demonstrated that patients with cirrhosis of the liver failed to excrete sodium in amounts adequate to achieve sodium equilibrium in spite of the maintenance of normal serum albumin by repeated injections of salt poor human albumin. Increased excretion of sodium followed the use of mercurial diuretics, or salt poor human serum albumin. It was also observed during a "spontaneous" decrease in ascites and edema formation. Restriction of salt in the diet decreases the rate of ascites formation and increases in salt in the diet lead to an increase in the rate of fluid retention.

It can be gathered from this discussion that edema and ascites formation in patients with cirrhosis of the liver is a complicated process. Portal hypertension, hypoproteinemia, the retention of sodium, reduced renal blood flow, delayed water absorption and water diuresis, increased intraabdominal pressure and hormonal factors are all important and contributing.

In the treatment of ascites and edema then the following points are important:

(1) Restrictions of salt intake.
(2) Replacement of protein deficits with whole blood transfusions or salt free albumin.
(3) Tapping the abdomen when there is increased ascitic fluid.
(4) Mercurial diuretics.

At any time during the course of cirrhosis of the liver but especially during the period when diffuse fibrosis is conspicuous and portal hypertension is greatly increased, hemorrhage from esophageal varices commonly follows. Aside from the

management of the acute blood loss, there have been developed during the past few years a number of surgical operations that are designed to shunt the blood from the portal circulation into the vena cava. The results of these operations have been truly remarkable. I shall not discuss them since other papers on this program will cover this subject. I have seen several of these patients operated upon by Dr. Smithwick and his associates and the results have been outstanding. Certainly these operations mark a further step forward in our management of cirrhosis of the liver.

Jaundice

There is no treatment for the jaundice in these patients. The intensity of the jaundice is a general index of the severity of the liver damage and the amount of intrahepatic biliary obstruction. The patients who are jaundiced are likely to show hemorrhagic phenomena so that all of these patients should receive adequate amounts of Vitamin K. Moreover, since the patients who are most deeply jaundiced are likely to have the greatest amount of fatty infiltration it is important to provide large amounts of glucose as well as protein in an attempt to displace fat from the liver and replace it with glycogen. The use of small amounts of insulin in these patients also appears to be helpful.

Summary

In considering any form of treatment of liver disease, it is well to consider the stage of the disease in which the patient is seen. When the liver is infiltrated with fat and enlarged without jaundice or ascites, then efforts should be made to correct the patient's dietary habits and provide him with adequate amounts of protein, carbohydrate and the amino acids that are lipolytic.

When edema and ascites are present, a diet low in sodium and an adequate protein and carbohydrate intake should be given. Whole blood transfusions, serum albumin, mercurial diuretics and abdominal tapping should be employed.

In patients with multiple gastric hemorrhages and good liver function, the question of portal caval shunt should be considered.

REFERENCES

1. Addison, T.: Observations on Fatty Degeneration of the Liver. Guys Hospital Rep. **1**:476, 1836.
2. Gilman, J. and Gilman, T.: Powdered Stomach in Treatment of Fatty Liver and Other Manifestations of Infantile Pellagra. Arch. Int. Med. **76**:63, 1945.
3. Conner, C. L.: Fatty Infiltration of the Liver and the Development of Cirrhosis in Diabetes and Chronic Alcoholism. Am. J. Path. **14**:347, 1938.
4. Rich, A. R., Berthrong, M. and Germuth, F. G.: An Experimental Enquiry into the Mechanism of Development of Cirrhosis of the Liver. Trans. Assoc. Am. Phys. **61**:263, 1948.
5. Best, C. H. and MacLean, D. L.: Choline and Liver Fat. Brit. J. Exp. Path. **15**:193, 1934.
6. Ralli, E. P., Leslie, S. H., Stueck, S. H., Shoor, H. E., Robson, J. S., Clarke, D. H. and Laken, B.: The Course of Cirrhosis of the Liver in Patients Treated with Large Doses of Liver Extract Intravenously. Medicine. **28**:301, 1949.
7. Himsworth, H. P.: The Liver and Its Diseases. Harvard University Press, 1947.
8. Myers, W. K. and Keefer, C. S.: Relation of Plasma Proteins to Ascites and Edema in Cirrhosis of the Liver. Arch. Int. Med. **55**:347, 1935.
9. Thorn, G. W., Armstrong, S. H. and Davenport, V. D.: Chemical, Clinical and Immunological Studies on the Products of Human Plasma Fractionation. XXXI. The Use of Salt-Poor Concentrated Human Serum Albumin Solution in the Treatment of Hepatic Cirrhosis. J. Clin. Invest. **25**:304, 1946.

9a. Kunkel, H. G., Labby, D. H., Ahrens, E. H., Shank, R. E. and Hoagland, C. L.: The Use of Concentrated Serum Albumin in the Treatment of Cirrhosis of the Liver. J. Clin. Invest. **27**:305, 1948.
9b. Falcon, W. W., Eckhardt, R. D., Murphy, T. L., Cooper, A. M. and Davidson, C. S.: An Evaluation of Human Serum Albumin in the Treatment of Cirrhosis of the Liver. J. Clin. Invest. **28**:583, 1949.
9c. Falcon, W. W., Eckhardt, R. D., Cooper, A. M. and Davidson, C. S.: The Effect of Human Serum Albumin, Mercurial Diuretics, and a Low Sodium Diet on Sodium Excretion in Patients with Cirrhosis of the Liver. J. Clin. Invest. **28**:583, 1949.
9d. Eckhardt, R. D., Falcon, W. W. and Davidson, C. S.: Improvement of Active Liver Cirrhosis in Patients Maintained with Amino Acids Intravenously as a Source of Protein and Lipotropic Substances. J. Clin. Invest. **28**:603, 1949.
9e. Patek, A. J., Jr., Mankin, H., Colcher, H., Lowell, A. and Earle, D. P., Jr.: The Effects of Intravenous Injection of Concentrated Human Serum Albumin upon Blood Plasma Ascites, and Renal Functions in Three Patients with Cirrhosis of the Liver. J. Clin. Invest. **27**:135, 1948.
10. Thorington, J. M. and Schmidt, C. F.: Study of Urinary Output and Blood Pressure Changes Resulting from Experimental Ascites. Am. J. M. Sci. **165**:880, 1923.
11. Bradley, S. E. and Halperin, M. H.: Renal Oxygen Consumption in Man During Abdominal Compression. J. Clin. Invest. **27**:635, 1948.
11a. Bradley, S. E., Ingelfinger, F. J., Groff, A. E. and Bradley, G. P.: Estimated Hepatic Blood Flow and Hepatic Venous Oxygen Content in Cirrhosis of the Liver. Proc. Soc. Exper. Biol. & Med. **67**:206, 1948.
12. McMichael, J. and Smivk, F. H.: The Effect of Experimental Portal Congestion on the Absorption and Excretion of Water. J. Path. & Bact. **37**:81, 1933.
13. Jones, C. M. and Eaton, F. B.: The Prognostic Significance of a Spontaneous Diuresis in Acute and Subacute Disease of the Liver. New Eng. J. Med. **213**:907, 1935.
14. Ralli, E. P., Robson, J. S., Clarke, D. and Hoagland, C. L.: Factors Influencing Ascites in Patients with Cirrhosis of the Liver. J. Clin. Invest. **24**:316, 1945.

Discussion

Dr. Fernando Biguria (Brookline, Mass.):—In his customary fashion, Dr. Keefer has discussed some aspects of the treatment of cirrhosis of the liver, clearly and concisely. I should like to speak about the variability of results in treatment.

We have all been perplexed by patients who, in spite of active and well-directed treatment, die; others, fortunately, respond in a very gratifying manner.

Comparing the two groups of patients, there appear to be no great differences. They may have large livers of the type that exhibits considerable amounts of fatty infiltration; they may have progressed further to varying degrees of fibrosis; they may have ascites; but I think an almost universal feature of the patients who do not respond well to treatment, is jaundice.

I don't think we have the final answer to explain why these patients do poorly, but it seems to me that a very important conditioning factor lies in the state of the intrahepatic circulation. It is easy to understand that if the medication which we give does not reach the target at which it has been aimed, and that is the liver cell, we cannot expect a satisfactory result.

Dr. Keefer has stated that fatty infiltration interferes with the passage of blood through the sinusoids; therefore the nutritious elements which we administer do not reach the liver cells due to the interference with the circulation. In the cases where fibrosis is present, that is even much more easily understandable, and we can postulate maybe two other situations where the sinusoid may be interfered with. In some stages of hepatic degeneration, the cells are swollen and therefore they infringe upon the sinusoidal space. Again, it is possible to think of such

overenthusiasm in the regeneration of liver cells that they may also interfere with the dimensions of the sinusoidal space and choke themselves to death.

It seems to me that the final answer will be provided only when correlation of pathological studies with clinical progress of the patient has established definitely in which ways and to which extent all these possible factors interfere with the intrahepatic circulation. I think then we may have made a very important step forward towards the correct treatment of this disease.

Dr. Charles S. Davidson (Boston, Mass.):—I should like only to emphasize two of the things that Dr. Keefer mentioned, with regard to the treatment of patients with cirrhosis who have ascites and edema. The first of these is with respect to the use of normal human serum albumin administered intravenously to such patients in an effort to raise their serum albumin concentration.

Our results with this were not satisfactory. We studied carefully some thirty patients. Of the thirty patients, only four had a prompt, dramatic diuresis with loss of a significant amount of ascites and edema. Also, of the thirty, six had no significant results which one could attribute to the administration of albumin. The remainder were more or less indeterminate, that is, one could not decide whether such factors as a good diet and bed rest, had made the improvement, or whether the albumin over the course of time was effective. In addition, we had some bad results.

Of the thirty patients treated, ten had quite bad results, and of those ten, four were fatal. Of the four fatalities, one was a fatal pulmonary edema, two had bleeding of the esophageal varices, and one an excessively severe nosebleed. Not only did we have these four fatal complications, but also we had a coincidence of bleeding from esophageal varices which was far above that which we would have expected under ordinary circumstances. We imagine that the increase in blood volume, following upon the administration of human serum albumin, presumably ballooned out the varices and made them more liable to rupture—at least we suspect that this may be the case. Thus, the good results were not as good as we might have expected, and the bad results were considerably more than we expected, so that we are not encouraged by the use of serum albumin as a therapeutic measure in patients who have cirrhosis of the liver and ascites and edema.

We are encouraged, however, with regard to the use of a low sodium diet.

In the first place, if you administer sodium to the patients with ascites and edema, whether you give it by mouth or intravenously, they retain the sodium in their body, or perhaps in their ascitic and edema fluid. At least practically none of it appears in the urine.

To do this requires the use of salt free protein, the most used of which are the salt free milk powders. With this régime one may effectively control the reformation of ascites and edema.

Dr. Horace W. Soper (St. Louis, Mo.):—This question is a very interesting one to me. I am glad to know that fatty infiltration of the liver was mentioned. We know that fat has high cholesterol content, and all the internal organs have a very high cholesterol content.

Now, as to the etiology of cirrhosis, over two hundred years ago the English physicians had a synonym for cirrhosis, namely, "gin-drinkers' liver". Gin was made in the by-products of the distillation of whiskey, and the people of England who drank good whiskey never developed cirrhosis, but those who drank the cheap gin, which contained the aldehydes and by-products of the distillation of whiskey, developed cirrhosis.

Now, you can't blame pure alcohol, aged alcohol, for the development of cirrhosis, but you can blame the unaged alcohol.

When I was an intern in the old City Hospital in St. Louis, we had an epidemic of cirrhosis from a barrel house which gave you a pint of whiskey for ten cents, and they drank it so rapidly it never had a chance to age. We had an epidemic of cirrhosis, and I was doing some of the work there.

When I was doing postgraduate work in Germany, in Berlin, the old pathologist would say, "Here is another case of Laënnec's cirrhosis. Well, Berliners don't get it. They may get a fatty liver; they don't get cirrhosis. What has this fellow been drinking? Schnapps!" Schnapps was an unaged whiskey consumed in the slums of Berlin.

Dr. Hyman I. Goldstein (Camden, N. J.):—Our youthful president, Dr. Soper, spoke of the "gin-drinkers' cirrhosis" of two hundred years ago! But, Galen (130-200 A.D.) discussed hepatic cirrhosis in his *"De Locorum Affectorum Notitia"*, Henricus Stephanus, Paris, 1513, p. 107 (obverse). He knew that *"Eteni quia ipsum, eius facultatis, que sanguine gignit, instrumenti est, consequés est, ut viciato hoc viscere, actio quocque eius vicietur"*—under "Scirrus hepatis". [". . . Since the liver is the chief instrument of the bloodmaking faculty, it follows that if this organ is diseased (or vitiated), also the function of this organ will be impaired or vitiated"]. During the past forty or fifty years, the Frenchmen, Paul Carnot, A. Gilbert, E. Vidal, Spillman, Maurice Perrin, Mouras, and others have advocated the use of liver therapy for cirrhosis of the liver ("Alcoholic"). With a good nutritious diet indulgence in some alcoholics will not lead to hepatic cirrhosis. That's why the Churchillian government leaders and statesmen do not develop ("alcoholic") cirrhosis of the liver!

In recent years, the late Charles Hoagland, Patek and Post, Keefer, Morrison, and others, have emphasized the need of a high protein and carbohydrate and vitamin-rich diet, the use of liver therapy orally and by injection! The reversibility of ("alcoholic") cirrhosis of the liver, and the recommended treatment of hepatic cirrhosis, was repeatedly stressed in the earlier French publications (1900-1910).

Dr. Samuel Weiss (New York, N. Y.):—I should like to ask Dr. Keefer these questions:

What experience, if any, do you have with injection of aspirated ascitic fluid?

Do you use intravenous liver injections in patients with cirrhosis and ascites?

Doctors McCabe and Hart, of the New York Polyclinic, have advocated the use of insulin, with good results.

On my Gastroenterological Service at the New York Polyclinic I inject intramuscularly 20 c.c. of the ascitic fluid every second or third day, in addition to intravenous liver, high protein, moderate carbohydrate and low fat diet, lipotropic substances containing methionine, and so forth, vitamins, diuretics, mercudem, mercuhydrin, salyrgan, fortified with B-Complex and large doses of C. If results are slow or fluid increases rapidly, abdominal paracentesis is repeated as indicated.

Dr. Chester S. Keefer (Boston, Mass.):—We have had no experience with the injection of ascitic fluid in these patients. We have had limited experience with the use of intravenous liver extract, but up to the present time we have not been impressed by the favorable results of using intravenous over intramuscular preparations. I think one can say that it is true that one can very often use a larger amount of liver extract intravenously than one can by the intramuscular route. In a number of patients who receive large amounts of glucose intravenously, we have combined it with small amounts of insulin.

THOUGHTS UPON DIABETES TODAY*

ELLIOTT P. JOSLIN, M.D.
Boston, Mass.

Gradually a new situation has arisen, because of the lengthening lives of the diabetics and the catastrophes into which so many fall after 20 years. This has led us to take back a group of older diabetics for a follow-up and a refresher course in diabetic treatment. This newest type of treatment which we have adopted for some of our patients has been that made possible in medical vacation diabetes camps. For 19 years we have had camps for diabetic girls and boys. During the two to eight weeks the children spent in these camps we were able to control diet, exercise and insulin and observe the good results, not only at the time but in the following year. Since such older patients are either in college or gainfully employed, we conceived the idea of offering older girls and young women a medical vacation to replace their usual vacation. In this way we could provide the pleasure and profit, derived from two weeks in the country, but, incidentally, inexpensive medical supervision and contacts with fellow diabetics with whom they could discuss their peculiar problems. Simultaneously, there was accessibility to medical advice, supported by modern laboratory facilities, and all this available without sacrificing time taken from jobs or studies.

The above plan, devised by Dr. Priscilla White, worked out very well this last summer and among the 301 diabetic children and young people in our two diabetes camps there were 17 young women who took advantage of this opportunity to bring themselves up to date in treatment. There were many more applicants than there were opportunities for patients. Indeed, among all of those afforded camp vacations, none were more grateful and enthusiastic than this special group.

Utilization of the vacation period for medical treatment can well be extended. Moreover, it can be made applicable not only for diabetics, but for other groups such as those with peptic ulcer. In a way the various European spas served a purpose along this same line, but with them the opportunities were chiefly for the well-to-do. Our demonstration at the Clara Barton Birthplace Camp in North Oxford showed that it is practical to offer such facilities on a larger scale. Today the cost of hospital treatment is almost prohibitive and, moreover, the need for hospital treatment of many patients with ambulatory disease is unnecessary. On the other hand, many of these ambulatory cases require most detailed supervision, such as diet and medical care, and this can be given in vacation camps at a far lower cost than would be possible in a hospital. In such camps the opportunity for exercise, pleasurable diversion and outdoor living are helpful accessories in the care of many patients.

The rules of treatment for diabetes last for life. I consider Dr. Sippy's greatest contribution to the treatment of ulcer of the stomach and duodenum to have been not the use of alkalis, but rather the emphasis he placed upon prolonged periods of treatment. His enthusiasm and his methods in driving this home to his

*Read before the Fourteenth Annual Convention of the National Gastroenterological Association, Boston, Mass., 24, 25, 26 October 1949.

patients and their doctors were of the greatest help to me not only in the management of the ulcer cases which I had at that period of my medical practice, but especially when I applied them to my diabetics. Medical vacation camps, whether for individuals with peptic ulcer or diabetes, I believe can be extended. They offer a great opportunity for recuperation, for rest, for instruction and for encouragement.

More than ever we believe in the aggressive treatment of diabetes of all types. For us there is no *laissez-faire* policy. Medical camp vacations keep this policy alive.

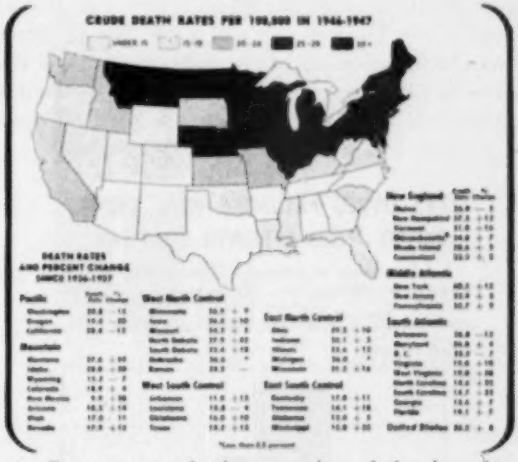
The class system is the method we try to utilize both at the hospital and in our office. The instruction of diabetics is not only an asset to them, but a necessity for us doctors. Granted that the greatest sermon in the world had only an audience of one, yet circumstances are such today that following a preliminary and intimate interview with our patients, we must resort to their instruction in groups. It requires some hours to teach a diabetic how he can live and a single recital of the rules of treatment does not sufficiently penetrate. When one has a small class of patients, then the questions of one person and the example of another will influence the diabetic neophyte often far more than what the doctor says. Moreover, this small class instruction can be extended to large groups. A few weeks ago before an audience of 1,100 here in Boston I think I accomplished more good in showing an attractive young woman, who had followed treatment explicitly for 27 years and was sound physically, had perfect eyes and the x-ray specialist found no trace of arteriosclerosis in her vascular system, than by anything I could have said to exhort those with diabetes in the audience to control their disease. She exemplified what could be done and I know I gave more hope to the diabetics in the audience than they had ever had before. Later I challenged the audience to produce anyone over 80 years of age and only one was present, whereupon I introduced a sprightly lady, born in 1855 and now 93 years and 10 months old, to whom I gave a gold medal, because she had lived twice as long with diabetes as she was expected to have lived if she did not have it. Class instruction could be utilized more with patients having gastrointestinal disease. More of you also should write short manuals of instruction in the management of gastrointestinal diseases for distribution among your patients and the laity in general.

You have heard much the last few weeks about the Diabetes Detection Drive. I hope you realize there was more bound up in that undertaking than appeared on the surface. In the first place, it was a notice to everyone in the United States that the doctors were donating their services. They were helping to discover new cases of diabetes so that treatment could be begun promptly. It was, moreover, done without subsidies from the Government and it was not a part of socialized medicine. That was the essence of the Diabetes Detection movement in my opinion, and worth far more to the United States than finding some thousands of new cases of diabetes. May I also point out that in this campaign there was no solicitation for funds, no asking for millions of dollars. The doctors in this drive were giving and not asking for money for medical research or medical care, excellent as those are.

What further concerns me in this Diabetes Detection Drive is not the discovery of new cases, so much as the necessity for the better treatment of existing diabetics as well as the newly discovered ones. Already there are plenty of diabetics to go around and we as a profession must adopt new rules for their care. On my farm today I don't use a pair of horses and two men to clear off the 400 loads of rocks per acre, but I use a bulldozer, and we doctors dealing with diabetics, and I suspect this same principle holds true for digestive diseases, must learn to employ new strategies and new personnel. Today there are not enough young doctors and nurses to do the work. Particularly we must educate a new generation of nurses' aides and young technicians who can do minor tasks and free the time of others, whose training has taken longer. From among these aides a few will be found who can assume considerable responsibility.

That I may give you an overall picture of diabetes today, as I see it, I am calling your attention to five tables, prepared for our exhibit with the Metropol-

TABLE I



itan Life Insurance Company at the last meeting of the American Medical Association and in part with the help of the Life Insurance Medical Research Fund.

The first table shows the statistical distribution of diabetes in the United States based on census death reports. I present this although it gives, in my opinion, a totally false impression. For example, the mortality of diabetes in Arizona is 10 per 100,000 and in New York State 40 per 100,000, but when I went to Arizona and visited every single town in the State above 3,000 inhabitants and interviewed each doctor in conjunction with the generous support of the Arizona State Medical Society, I found actually there were just as many diabetics living in Arizona as in the East. Instead of no diabetics among the Indians, I discovered by blood sugar and urine tests, with the help of officials of the Indian service, 71 Indians with diabetes. If one makes allowance for accessibility of the inhabitants to the gathering of statistics and their reliability, for the age and sex of the inhabitants,—it takes

approximately two thousand children to get one diabetic but 45 women above 65 years—the incidence of diabetes in the United States, in my opinion, is just the same in one part of the country as another. As yet, in no town in the United States or in any country has there been a survey comparable to that conducted by the United States Public Health Service in Oxford, in which 3,516 of the 4,983 people were tested for diabetes.

TABLE II

AVERAGE DURATION FROM ONSET TO DEATH IN SUCCESSIVE ERAS OF TREATMENT YEARS

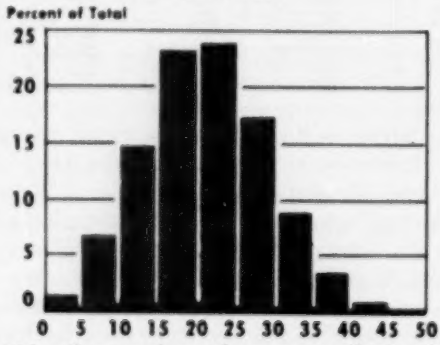
Age at Onset	Naunyn Era	Allen Era	Banting Era		Hagedorn Era	C. H. Best Era
(Years)	1897-1914	1914-1922	1922-1929	1930-1936	1937-1943	1944-1949
All Ages	4.9	6.1	8.0	10.4	12.5	14.4
Under 10	1.3	2.9	2.8	7.3	10.3	18.3
10-19	2.7	2.7	3.4	7.5	11.5	15.6
20-39	4.3	4.9	8.9	14.4	16.9	18.7
40-59	7.0	8.0	9.5	11.7	13.8	15.6
60 & over	4.4	6.4	5.5	7.1	8.8	9.4

This second table represents the culmination of my work with diabetics thus far. It is based upon the 10,673 diabetics whom I have seen but who subsequently died. Please look at the first line and you will notice that in succeeding periods of time, as one follows the figures from left to right, the average duration of life of diabetics has risen to be 14.4 years, or three times as long as it was prior to 1914. Today the average diabetic lives a little over 14 years after his disease is discovered and at no decade of onset does it exceed 18.7 years.

TABLE III

2145 LIVING PATIENTS* WITH ONSET BEFORE THEIR FIFTEENTH BIRTHDAY

Experience of George F. Baker Clinic
Analysis by Metropolitan Life Insurance Company

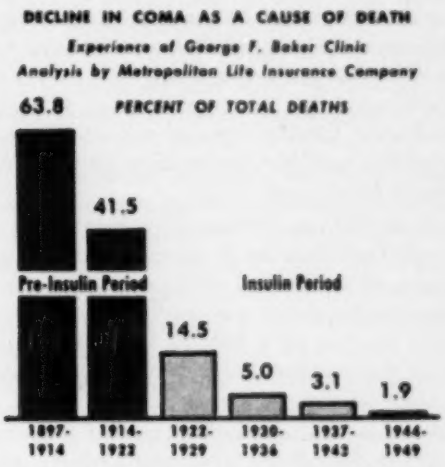


This table would be discouraging unless one recalls that it is made up of dead diabetics and not of living diabetics, and to bring out that point may I for contrast present Table III.

This shows that there were living in 1948, 2,145 diabetics with onset before their fifteenth birthday, and you will note that approximately 25 per cent of the

total have lived to be over 20 years of age and that a few of these patients already have reached 50 years of age or, in other words, have had diabetes over 35 years despite the fact that it began in childhood. The diabetics who have died within the last five years with onset under 10 years of age lived 18 years, but there were only 46 of them. Another reason the average duration for all diabetics is 14.4 years is that when one takes ten thousand diabetics, a large proportion of them develop the disease after the age of 60 or 70 years when their expectation of life is short and that handicaps the total. In one country of Europe recently, 136 cases of diabetes with onset in childhood were reported (49 untraced), but not one of these cases has lived over 21 years.

TABLE IV



There is still much discussion about diabetic coma and its treatment. Table IV shows our experience beginning with 1897-1914, when approximately two-thirds of our patients died of it, in contrast to now, when it has dropped to 1.9 per cent. This figure relates to our cases dying anywhere in the world. The latest figures for our last 132 cases with CO_2 values of 20 volumes per cent (9 millimols) or below, treated in the George F. Baker Clinic at the New England Deaconess Hospital, show a mortality of 3.0 per cent. Our improvement in treatment over the years is in the prompt use of insulin in the first three hours, the employment of salt solution to combat dehydration, lavage of the stomach to avoid the dilatation of that organ, and concentrated nursing care. In the last 32 years we have not used alkalis, glucose or potassium. In fact, there are very few, if any, cases of diabetic coma in which potassium is needed or has been extremely low unless the patient has been given glucose along with insulin medication in the first few hours after admission to a hospital. Give insulin freely and early, omit glucose and potassium will not be needed.

TABLE V

VASCULAR COMPLICATIONS RISING WITH DURATION DIABETES IN YOUNG DIABETICS
202 Cases With Onset of Diabetes
Between Ages 15 and 30

Duration (Years)	0 - 10	11 - 20	21 - 29
High Blood Pressure (%)	2	21	33
Calcified Arteries (%)	21	66	88
Retinitis (%)	4	56	60
Average Age (Years)	28	39	47

Growing old prematurely is the bane of diabetics today. Instead of two-thirds dying of diabetic coma, at present two-thirds, whether young or old, die of arteriosclerosis. My colleague, Dr. Priscilla White, has brought this out very clearly with children. The incidence of vascular changes in the eyes has been emphasized for all ages by Dr. Dolger, but there is another study of 202 cases with onset of diabetes between the ages of 15 and 30 years by my colleagues, Dr. Howard F. Root, Dr. Richard Sinden and Dr. Ralph Zanca, to be published, which is worthy of your attention. In this table you will note that only 2.0 per cent of the diabetics with 10 years' duration had a high blood pressure, but 33 per cent showed it after 21 to 29 years of the disease. Calcified arteries were present in only 21 per cent in the first 10-year period but in 88 per cent at 21 to 29 years, and retinitis likewise rose from 4.0 per cent to 60 per cent.

Arteriosclerosis is the burning problem of diabetes today, but we should not lose sight of the thought that there are at least 20 diabetics in the United States, treated in various clinics, who at the end of 25 years showed none of it whatsoever. It is only 22 years ago that Lindbergh was the first and the only one to have flown the Atlantic, but during the first six months of 1949, 149,526 passengers crossed it in American airlines. If that number of diabetics win the Victory Medal also after 22 years, I shall be quite satisfied.

We know that the cases most aggressively treated with orthodox methods are the ones who have earned the Victory Medal and I believe it true to say that for every year added to the average life of the diabetic in this country, what is learned thereby in the prevention of arteriosclerosis will make it possible for a year to be added to the lives of the other 148,000,000 of nondiabetics. Teach a diabetic with his predilection for arteriosclerosis to live a year longer and then apply similar methods to nondiabetics.

Finally, may I bring up one thought which I hope will reach every doctor in the world who treats a diabetic. I know of no group of patients with any disease who are followed for so many years and who are under such close and such long medical supervision as the diabetic. Diabetics constitute the best group by which to evaluate the value of health examinations. This group in our community should show to the highest possible degree the advantages of routine and frequent health examinations. I tell each of my patients, when they go to see their doctor, to take off all their clothes so they can be examined from foot to head, with the idea that if there is any disease other than diabetes it will be discovered early. That applies particularly to tuberculosis in Europe, but to cancer in this country. A delayed

diagnosis of cancer in a diabetic reveals the doctor to be derelict in his duty. The diabetic should be the one in which cancer is found earliest. Favorable cases for operation of cancer of the stomach or of the bowels, such as the diabetics present, should be detected earliest among our diabetic clientêle. All of us who treat diabetics should realize that surgeons know this and that they are holding us strictly responsible for an early diagnosis. I want the time to come when doctors treating diabetics and diabetics themselves can challenge the world by presenting the best statistics known for the cure of cancer.

Discussion

Dr. David Adlersberg (New York, N. Y.):—It is always a privilege and a pleasure to listen to Dr. Joslin. I have heard him many times and on each occasion I had to admire his ability to present new facets and new ideas to the problem of diabetes mellitus to which he has devoted his life's work.

I was particularly interested in Dr. Joslin's idea of vacation camps for ulcer patients in a similar manner as we have them for diabetes patients, especially children. Diet regulation remains the important weapon in the therapy of both diabetes and peptic ulcer.

When I received the invitation to discuss Dr. Joslin's address, I speculated on the more important gastroenterological problems in diabetes. If I may have a few minutes of your time, I should like to say something on them.

Our problem begins with the oral cavity of the nontreated diabetic. The dentist who is aware of these changes (spongy gums, pyorrhea) is the one who, not infrequently, discovers diabetes. We all know that the status of the oral cavity in the diabetic is a good index of the patient's control.

Another problem of interest is gastric acidity in diabetes. There has been a great deal of speculation and controversial opinion on this topic. Since insulin stimulates gastric secretion, it was thought that diabetics should present higher incidence of achlorhydria and achylia than nondiabetics; but something must be wrong in this speculation. By now, it is well established that achlorhydria occurs approximately as often in diabetics as in nondiabetics.

We also do not believe, as was thought some years ago, that peptic ulcer is rarely observed in diabetics. A considerable group of peptic ulcer carriers, especially of the duodenum, has been seen by us and others.

A very important chapter is abdominal pain in diabetic coma, and I am sure that Dr. Joslin is going to discuss this problem in the postgraduate course which will follow this meeting. It may be a very difficult diagnostic problem to differentiate an acute abdomen caused by acute cholecystitis, or acute appendicitis, or acute pancreatitis, from those severe abdominal pains that may be observed in advanced diabetic acidosis without any of these acute conditions. On the other hand, any of these conditions may be the precipitating factor of diabetic acidosis and coma.

I feel the physician is justified in rapidly treating acidosis with insulin, fluids and so forth. If the abdominal symptoms are due to diabetic acidosis per se,

then pain and fever will subside with control of diabetes and the restoration of normal acid-base and fluid balance. If the abdominal symptoms persist, and e.g. center around the appendix, then the surgical approach is indicated. In the meantime, the patient was rapidly prepared for surgery by proper care of the diabetes and re-establishment of acid-base and fluid equilibrium.

I should like to add that the modern treatment with antibiotics has changed the situation to a great extent, and that with the use of penicillin, streptomycin, aureomycin, etc., these important decisions ("to operate or not to operate") are not as urgent as they were only a few years ago.

A very important clinical problem is diarrhea in diabetes. When a diabetic has diarrhea, one has to search for a pathogenic organism responsible for the diarrhea in the same way as we do it in nondiabetics. We have recently seen a group of diabetics in New York City who had amebic dysentery. Only occasionally does one find real steatorrhea in diabetes. In contrast to sprue, the stools are loaded with neutral nonhydrolyzed fat, while in sprue only a small fraction of the stool fat is neutral fat, and the greater portion consists of fatty acids and soaps.

There are, however, cases of recurrent diarrhea in diabetics without any evidence of tumor, enteritis, or colitis or any other of the known causes. Still, I do not believe that this form of diarrhea occurs more frequently in diabetics than in the general population. A diabetic may be exposed to what is being commonly called "an upset stomach" just as frequently as a nondiabetic and a diarrhea that we cannot account for is a frequent occurrence in medical practice.

I think time does not permit me to go into the problem of cholecystitis, cholelithiasis and pancreatitis in diabetics. These conditions are of common interest to both the gastroenterologist and the physician interested in metabolic diseases.

Dr. Henry Baker (Boston, Mass.):—I have listened to Dr. Joslin talk, on many occasions, with keen interest, but this afternoon I listened very carefully to his presentation in order that I might properly discuss his paper, since I did not know exactly what he was going to say.

All his talks in the past have had at least one common denominator, and that is his optimism and his faith in the future of the diabetic patient. This, may I call it, "Joslin creed", first showed its importance in the preinsulin days. A few of you may remember that not only the patients but also the doctors themselves were greatly discouraged about the outlook in the treatment and the future of the diabetic. You saw the charts of the mortality before the days of insulin and the present-day mortality, and so, with that mortality before insulin, of approximately 63 per cent, that is, in coma, one can see how the doctors in that period were greatly discouraged.

Were it not for Dr. Joslin's optimism and faith in the eventual control of this disease, many a patient and doctor would have given way to despair. With the advent of insulin and now the newer types of insulin, Dr. Joslin's faith is being justified. How many patients and even doctors would have believed that today some diabetics can get insurance coverage, even though it may be at a higher rate?

This afternoon again you have heard Dr. Joslin expressing his views with the same enthusiastic optimism which is now paying dividends, so today the diabetic régime consists of a carefully calculated diet, sufficient exercise, insulin as needed, and a goodly portion of Joslin optimism. Early diagnosis is important in all diseases, not only in diabetes. Doctors are very keen to observe and to react very quickly if a patient has an acute surgical abdomen or a severe hemorrhage, or any other acute episode. A chronic disease, on the other hand, is too frequently neglected and treatment postponed, since the patient may have certain signs and symptoms over a long period of time which do not handicap him too greatly in his daily activities.

This is especially true in diabetes, since it is well known that an adult may have hyperglycemia and glycosuria for long periods of time without greatly incapacitating the patient; up to the acute stage of moderate or severe acidosis or even coma, a *laissez-faire* attitude is too commonly adopted. Those of us who treat many diabetics have seen complications and severe vascular damage which might have been avoided if early diagnosis had been made and adequate treatment instituted.

Several diabetics, as you have heard from Dr. Joslin a few moments ago, have gone along for a number of years without vascular degeneration in excess of what might be expected for their age, because early diagnosis of diabetes was made and proper and continuous treatment was carried out.

Of course, in one of the other tables we did see a number of cases develop vascular changes after a period of years, despite insulin diabetic treatment. In order to reach our goal, proper education, more alertness and awareness by both patients and doctors, are necessary.

Some of the patients who have benefited by this régime have already received, as you have heard, the Victory Medal from Dr. Joslin, and I suppose it may be possible, Dr. Joslin, if the program is carried out as you would like to see it, that you will cause a boom in the gold and bronze medal industry, as well as an increase in the life expectancy of patients, and in the well-being of the diabetic population.

So far as mass treatment is concerned, we all believe that proper and adequate treatment should be available to all patients suffering from any disease; however, the method of mass attack on any disease may be subject to the various views as to whether it should be done by the Government, as socialized medicine, or by the medical profession on an individual basis. Here in Boston we have several well-organized and well-equipped clinics for both in- and outpatients to take care of the indigent diabetics. Also available is a free district home service.

In our outpatient clinic at the Boston City Hospital we also supply the patients with their insulin, syringes, needles, and so forth, for home use, at no cost to them whatsoever. The patient has only to supply himself with proper dietary requirements. If he is unable to do so, he then becomes a welfare problem, as well.

In Boston all known diabetics can receive good medical attention under any circumstances. The basic problem is to find the unknown diabetic.

I am sure that all large cities have similar plans. I am greatly interested in these classroom instructions which Dr. Joslin gives his patients, and I think that plan ought to be adopted more universally in the various hospitals, and also the refresher courses for the adults in the camps I think are extremely important for our patients. I only wish there were more camps where more of our patients could go.

The juvenile vacation camp I think is extremely important. The value of such a camp is three-fold: First, children lose diabetic self-consciousness; second, they gain self-reliance; thirdly, they develop self-confidence.

A youngster who has diabetes very frequently shies away from other people and is afraid they will think he is not like other children. Many of them have an idea that anyone can tell by looking at them that they are diabetic and somehow different. In this camp, surrounded by other children who also have diabetes, such a child loses his diabetic self-consciousness. Life in a diabetic camp gives a child an opportunity to take care of his diet and insulin away from home and parental supervision. At camp he is given an opportunity to feel that he can check his own diet and insulin, and that he is on his own. This makes for a feeling of self-reliance.

Camp life also gives the child a chance to discover that he can enjoy the same activities as other children of his own age, and he develops self-confidence.

I should like to go a step further in the vacation camp program by suggesting that before the end of the summer the diabetic child be sent to a camp with non-diabetics, so he will have the opportunity to carry out his régime in a different environment. If he has a feeling of self-consciousness, it will be greatly dispelled when he realizes that to an outsider who may visit this type of camp, he looks as normal and healthy as the other children. This factor, plus his ability to carry on the usual activities with the rest of the boys, will instill confidence in his ability to take his place in society.

Since he has already been trained in the selection and amounts of food, his insulin therapy and its reaction, this nondiabetic camp will help prepare him for the future, when he may have to take his meals away from home, as in restaurants, while at school, or on a job. All these factors are very important in the mental and physical outlook of the patient.

Dr. Joslin has zealously and continually accumulated all available data, including the latest research developments in diabetes concerning its mechanism, diagnosis, and treatment. With his wisdom he has applied this knowledge clinically with remarkable success and to the benefit of mankind. For this we all owe him a debt of gratitude.

Dr. J. Edward Flynn (*Boston, Mass.*):—It would be very presumptuous on my part to attempt to discuss the material in Dr. Joslin's fine paper. I will confine my remarks to a few of the aspects in the surgical treatment of the diabetic patient.

There are four conditions which may be associated with diabetes, which are of particular interest to the surgeon: carbuncle, gangrene of the lower extremity, appendicitis, and cholelithiasis. Every attempt should be made with the diabetic

patient to avoid an emergency surgical operation. Every diabetic patient will be improved and will be better evaluated by a period of care in the hospital. This is particularly true of the diabetic patient who has not received previous treatment for his diabetes. Standard, Brandalion and Raleigh report a mortality of 6.9 per cent in the diabetic patients previously treated for the disease, and a mortality in the diabetic patients not previously treated for diabetes of 20.8 per cent.

The basic principles in surgery in diabetic patients are an accurate diagnosis, a careful evaluation, a patient and determined and deliberate preparation of the patient for the operation, a thoughtful selection of the anesthesia, a carefully planned and carefully executed operation, followed by a detailed postoperative medical and surgical follow-up. Adherence to these details will result in a mortality in the diabetic patients who undergo surgery approximately the same or slightly higher than in the nondiabetic patients who undergo surgery for similar conditions.

The surgical gastroenterologist is interested in carcinoma, as Dr. Joslin has well pointed out, and he also pointed out how the diabetic patient who is being treated might have his cancer picked up at an early stage.

I believe the surgical gastroenterologist is interested mainly in two other diseases, appendicitis and cholelithiasis. Appendicitis is a most serious matter in a diabetic, more serious than in the nondiabetic. The diagnosis may be masked in a diabetic patient. The acidosis may produce marked signs and symptoms of appendicitis—vomiting, fever, and a leucocytosis, and tenderness in the right lower quadrant. Many of these patients have been explored without a finding of cause for the symptoms in the abdominal cavity.

Peritonitis is a most serious condition in the diabetic, more serious than in the nondiabetic. The infection is harder to control in the diabetic patient. Every attempt should be made to get control of the diabetic state before the patient is submitted to operation; however, if the surgical lesion is such as to render this hazardous, then we believe that operation should not be delayed.

Children with diabetes will commonly have recurrent attacks of abdominal pain unassociated with acidosis. It is extremely hard to evaluate the role of the appendix in these patients. Many of these children have been operated upon without finding the cause for the symptoms that they presented, particularly recurrent attacks of abdominal pain; however, on the other hand, diabetes in a child may mask the symptoms of appendicitis, and many of these children with appendicitis and diabetes have had rupture of the appendices and died. It seems wise that when explanation cannot be made on any other basis, an exploration should be performed and the appendix be removed, even if it is a white appendix, rather than run the risk of having an emergency procedure under any circumstance, or run the danger of missing the diagnosis of appendicitis.

Gallstones are, generally speaking, more common in a diabetic than in a nondiabetic patient. Gallstones probably are not a factor in causing diabetes, and a patient who has gallstones, who has his gallbladder removed, and has diabetes, has no decrease, probably, in the severity of the diabetes.

Recurrent attacks of cholecystitis, particularly that type which is associated with a secondary infection, will upset the course of a diabetic patient as will infection elsewhere upset the course and management of diabetes. Acute cholecystitis is a more serious disease in the diabetic than the nondiabetic. It tends to subside less than it does in the nondiabetic. The incidence of necrosis and perforation is greater in the diabetic than in the nondiabetic, so we feel that early operation is indicated in the patients with acute cholecystitis. The presence of gallstones is probably an indication for operation, with everything else being equal, if the patient is in relatively good general condition. An early diagnosis of gallstones and elective operation performed under ideal circumstances will probably decrease the incidence and complications, and decrease the mortality in this group.

The next group is the patients with recurrent cholecystitis without stones. We feel that these patients should not be operated upon, because operation for chronic cholecystitis in a patient who does not have diabetes is too uncertain in its outcome, and the value of it is too uncertain, so we prefer not to submit the diabetic patient with so-called chronic cholecystitis without stones, to surgery.

I should like to ask Dr. Joslin one question: How should we treat the patient with a ruptured appendix and appendiceal abscess? Previous to the antibiotics, the mortality with this condition was 40 per cent. Should we treat these patients for their diabetes, give them antibiotics, and treat them conservatively, hoping for a resolution of the abscess, or should we treat the diabetes, give the patient antibiotics, and perform incision and drainage for the abscess?

Dr. Elliott P. Joslin (Boston, Mass.):—I am very grateful to the first speaker for bringing up possibilities as to what we might do for these children in camp in building up morale and testing them out, possibly, in other camps. It is worth a great deal to have that mentioned.

Secondly, the speaker spoke of the surgeon. At the course in Gastrointestinal Surgery I shall discuss our ulcer and cancer cases and the emergencies accompanying them and also occurring with diabetic coma: (1) dilatation of the stomach; (2) hematemesis. Perhaps it isn't right to say "hematemesis" because they may not vomit, but if you put a stomach tube down, you will find old blood in the stomach, and sometimes you may find you have old blood in the stomach and an ulcer, too; (3) symptoms of pain in the abdomen, and so many times the question of appendicitis comes up. I think I am surely telling the truth when I say that two out of three of our cases of coma are seen by a surgeon in consultation, and I am sorry we call them up at midnight and early in the morning, but with children we just don't dare take the responsibility ourselves, and these surgeons are so kind as to help us out.

Then there is the question of ulcer. I quite agree with the last speaker, it is far more common than we used to think—the fallacy of statistics! I will go into that at the Course also.

For that paper I have had the help of Dr. Risley, who has been with Dr. McKittrick for a considerable length of time, and he has looked up all our cases

of complications in the stomach and intestines for the last nine years. I will try to summarize these with his help, and I am hoping that we will be allowed to publish the article together, because he has brought a great deal of study to it.

There is just one point about the association of surgeon and doctor in diabetic cases. I am glad to talk about that, because for the fifty years in which I have dealt with the surgeons we have one rule, and the rule is that so far as possible we call the surgeon early and we tell him to do anything that he thinks should be done and forget the diabetes, because it is our job to match his surgical efforts with medical care. I can honestly say in all these years we have never regretted this practice.

The surgeon who treats a diabetic is a most courageous man, because he must operate on people who, after ten or fifteen years of the disease, are really riddled with arteriosclerosis. I wonder sometimes how they dare to do it.

THE ANTIBIOTICS IN GASTROINTESTINAL DISEASES*

MAXWELL FINLAND, M.D.†
and
E. BUIST WELLS, M.D.††
Boston, Mass.

The use of chemotherapeutic and antibiotic agents in the treatment of enteric infections was discussed.

In the case of typhoid fever some favorable results have been reported from the combination of penicillin and sulfathiazole (or sulfadiazine) by some British workers. The results obtained by others using this treatment in Britain and in this country have been equivocal. Streptomycin, likewise, has failed in typhoid fever in spite of the sensitivity of the organism in vitro and in spite of the fact that resistant strains of typhoid organisms do not emerge during the treatment of this disease as it does in most other infections. Aureomycin has given some favorable effects in typhoid fever, but the over-all results have been equivocal. Polymyxin is the most effective of the antibiotics in vitro and has occasionally proved life-saving, but it is too toxic for use except under the most carefully controlled conditions. On the other hand, chloromycetin in full doses has quite regularly resulted in rapid resolution of fever and symptoms. Relapses of fever and symptoms with bacteremia and positive stool cultures have been observed rather frequently, and perforation and hemorrhages have occurred after apparent clinical improvement following chloromycetin therapy. Chronic typhoid carriers have not been cleared either by chloromycetin or by any other known agent.

Salmonella infections other than typhoid fever have failed to respond clinically or in experimental animals to available agents. Bacillary dysentery, on the other hand, has been favorably affected by streptomycin, polymyxin and aureomycin and possibly by chloromycetin. The sulfonamide drugs, however, have proved to be the agents of choice in the therapy of bacillary dysentery. Sulfadiazine has proved to be superior to the nonabsorbable sulfonamide in this respect.

There are preliminary reports of the favorable effects from some of the new antibiotics in the treatment of amebic dysentery with elimination of parasites at least from the bowel contents. There is little information concerning their effects on localized lesions other than those on the surface of the bowel.

In tuberculous enteritis the more recent reports indicate that the disease is favorably influenced in many cases by streptomycin. However, relapses and progression of the disease have occurred in increasing numbers of cases following the conclusion of therapy as the period of observation and follow-up has increased.

---

*Abstract of a paper read before the Fourteenth Annual Convention of the National Gastroenterological Association, Boston, Mass., 24, 25, 26 October 1949.

†Associate Professor of Medicine, Harvard Medical School; Chief, Fourth Medical Service, Boston City Hospital; Associate Physician, Thorndike Memorial Laboratory, Boston City Hospital.
††Research Fellow in Medicine, Harvard Medical School and Boston City Hospital.

In ulcerative colitis, in spite of some favorable reports by a few observers, the results of the chemotherapeutic and antibiotic agents have, in general, been equivocal.

Discussion

Dr. Francis T. Jantzen (Boston, Mass.):—I shall limit myself briefly to some remarks upon the use of the sulfonamides in surgery, especially the surgery of the lower bowel.

The sulfonamides, to the surgeon doing intestinal surgery are still a very great source of comfort, especially the lower down he goes in the gastrointestinal tract, and more particularly if he finally gets into the big gut. Here, because of the fact that the sulfacetimides, particularly sulfasuxidine, and now sulfathaladine, have very little absorbability, it is possible to obtain a preoperative field that can even be made sterile; in other words, one can get sterile intestinal contents. The rate of absorption is so low, apparently, that they have no effect on the hematopoietic system and no effect upon the kidneys themselves. In fact, it is hard at times to detect any blood concentration, and I have never known of a case in which we actually found crystals in the urine under the use of sulfathaladine. You can in the course of five days usually obtain a sufficiently sterile field to enable you to do surgery in one stage that prior to these drugs you would have divided into two stages.

This, of course, is a great comfort to the patient, to have after five days of approximately four grams to each day, the ability to look forward to only one operation instead of two, as was frequently the case formerly.

Dr. H. Allan Novack (Boston, Mass.):—One thing that I believe I will take away with me from Dr. Finland's dissertation is the fact that typhoid fever still does exist. When I was a house officer at the Boston City Hospital, and that was back in 1922, it was rather unusual for us to see more than one, or perhaps two cases of typhoid fever a year. Dr. Finland has shown us a good many and, from my point of view, which is an interest in the public health part of this subject, I wonder what their origin was. I wonder what the public health aspect, especially of the childhood typhoid fever, is. I hope Dr. Finland will take a minute to tell us a little about that.

In my discussion I am going to say a word about the enteritis that occurred so frequently during the war, in North Africa, in Italy, especially the infestation with Shigella.

We know that with the use of streptomycin there has been a considerable advance in the treatment of the gram-negative enterobacteriæ, mainly the coliform varieties. Strains of different members of this group of bacteria have been very carefully and thoroughly studied recently by Dr. F. P. Roland, formerly of the Pasteur Institute, now working with Dr. Walter J. Nickerson, at Brown University. He has found that these strains produce substances among their metabolic products which have been shown to possess antibiotic action against other members of the same family, most frequently members of the Shigella group.

Three different antibiotics have been discovered, or, to put it better, isolated, and these can be differentiated on the basis of their reactions to heat, Seitz filtration, and to treatment with proteolytic enzymes. These antibiotics have compared very favorably with streptomycin, and to date they have afforded some, though not complete, protection to mice inoculated with Shigella. I might say that in vitro they have shown considerably more activity than they have in vivo, as is usually the case. Perhaps as they are further purified they may be used with greater effect in combination with streptomycin.

These newer antibiotics, as well as the older streptomycin, as we have been aware, cause the development of resistant strains of the Shigella, and Dr. Roland has recently shown that these resistant strains have a different antigenic structure from the parent strain. While resistant strains of Salmonella develop also, these latter strains of the Salmonella group—and I think this is quite important—have thus far been of the same antigenic structure as the parent strain. This finding for the Shigella, the fact that they are of different antigenic structure, is of very considerable interest, and may indicate something of the mode of action of the antibiotics.

Now I want to say just a word about tuberculous enterocolitis. The primary type of this disease, since the eradication of infected cattle and the elimination thereby of the bovine tubercle bacillus, is practically unknown in this country. The incidence of the secondary type of tuberculous enterocolitis has dropped markedly in the past twenty years, at least, since the advances in and the more general employment of collapse therapy, with the resultant elimination of so many cases of positive sputa. It is surprising, therefore, that more intestinal tuberculosis does not occur, considering the vast numbers of tubercle bacilli that are swallowed by patients with pulmonary tuberculosis, as evidenced, as you are all aware, by the frequency of positive gastric contents where sputa were repeatedly negative.

In our laboratory we have shown that the viability and the virulence of tubercle bacilli depend strictly upon the length of exposure to gastric juice. The longer the exposure, the less likelihood of culturing out the tubercle bacillus.

We have for many years used the enterogastric tube for inoculation of guinea pigs with tuberculosis, and have usually been able to give them extensive disease with only two small intragastric feedings, using about a hundredth of a milligram of the RV strain of H-37, feeling that this method, the intragastric method, is more akin to the human manner of contracting tuberculosis.

These animals were always, of course, tuberculin-negative to start with, but, even in them, we have never encountered tuberculosis of the stomach in all of our numerous autopsies. The commonest location of this type of enterocolitis is in the ileocecal region, more likely the terminal ileum than the cecum; and not infrequently the appendix is involved. Any tendency to intestinal stasis can be considered a predisposing factor to the formation of tuberculosis of the colon; therefore, constipation must be avoided.

Also, as a preventive measure, there must be—and this has been shown quite definitely—an adequate intake of Vitamins A, C, and D, avoidance of any factor

that would be irritating to the intestinal mucosa, thereby allowing a possible source of entry of the tubercle bacillus.

The emotional aspect must be considered also as a possible predisposing factor of the disease itself, but when that phase is marked, then you frequently get a very severe type of enteritis, and it is frequently mistaken for tuberculous enterocolitis.

In the last few years the most potent weapon we have had to combat this disease has been streptomycin, but that alone will rarely improve more than 50 per cent of the cases. It is felt that adequate therapy must include all the measures we usually employ in the so-called nonspecific ulcerative colitis, together with the antibiotic, and any indicated pulmonary collapse therapy. The latter, of course, without saying, should be instituted promptly in every case of pulmonary tuberculosis of an active nature.

The psychosomatic element in tuberculosis is always very important, and when symptoms of enteritis begin to appear, that phase should be given a large share of attention. In addition, active treatment should be fairly vigorous and should include proper rest for both the pulmonary and the enteric disease, and adequate but smooth diet with the addition of hydrophilic emulsoid of psyllium, which we have found rather effective in some respects; drugs, chiefly of the antispasmodic groups, with the addition of mild sedation. Heliotherapy has been used a good deal. It must be very carefully applied, using the Rollier technic with avoidance of direct exposure to the chest. Oxyperitoneum in preference to straight pneumoperitoneum, and the utilization of about 300 to 600 c.c. of oxygen per week, in weekly doses, has been very effective. In some acute cases of tuberculous enterocolitis, two or three a week for perhaps two months, has sometimes practically eliminated all signs and symptoms of the disease. There are simpler things, such as abdominal heat and avoidance of all chilling; cold drinks should be excluded.

Surgery, except where the disease has been confined to the appendix, has been most disappointing unless it has been an emergency surgical procedure in the nature of a perforation or hemorrhage or obstruction due to stenosis.

Dr. Hyman I. Goldstein (Camden, N. J.):—This presentation by an expert on the use of the many sulfa preparations, and now, on the use of penicillin, streptomycin, chloromycetin (from streptomyces), aureomycin, neomycin, bacitracin, gramicidin, tyrothricin, and several other antibiotics, is of importance to internists, gastroenterologists, surgeons, and general practitioners.

The treatment of ulcerative colitis by vagotomy, antibiotics and sulfa drugs, by "psychosomatic medicine", and by various other surgical procedures, ileostomy, colostomy, and partial or total colectomy give evidence that we still must look to the future for better knowledge of the etiology and successful treatment of these colitides!

I hope Doctor Finland will discuss the use of antibiotic therapy in colitis, ileitis, biliary tract infections, and in the complications that may arise in the course of active ulceration of the gastrointestinal tract.

May I remind you that John Tyndall, in his laboratory, found that penicillium glaucum killed and rendered dormant and quiescent the bacteria in the tubes growing on various media (1874-1876)! This was seventy-five years ago!

It is unfortunate that Tyndall's observations were not followed by experimental and clinical application of the discovery of the bactericidal and bacteristatic effects of pencillium. Even the terms "Antibiosis" and "Antibiotic" were known in 1889—and P. Vuillemin's article should be re-read, along with the publications by C. V. Cornil and V. Babes (1885), and Link's "Observationes" (1809). Link first applied the name "penicillium" to a genus of green molds and fungi—and described three species of this genus: Penicillium glaucum (with which Tyndall caused the bacteria to die, and become dormant "as a slime of dead and quiescent bacteria" and "caused by the clay layer of penicillium"!), penicillium candidum and penicillium expansum—one hundred and forty years ago! Florey and Fleming, as you know, worked with penicillin from penicillium notatum. Let us hope that some of our newer antibiotics, and a better understanding as to the etiologic processes involved will lead us to have more successful results in the management of idiopathic ulcerative colitis, stenosing regional enteritis, and other forms of granulomatous and ulcerative disease of the gastrointestinal tract,—and perhaps, the "collagen diseases", now being treated with ACTH, Cortisone, and Compound E, may point the way!

Dr. Maxwell Finland (Boston, Mass.):—I am afraid I didn't mention ulcerative colitis because the results have been variable with all forms of therapy. Perhaps those of you who are interested in coming to the postgraduate course, will hear something more on this aspect.

RECURRENT INGUINAL HERNIA*

ROGER T. DOYLE, M.D., F.A.C.S.
Boston, Mass.

Recurrent inguinal hernia is a condition that appears to become progressively less of a problem. The rate of recurrence, however, still causes dissatisfaction among many of our present day surgeons. This fact is borne out by the abundant literature each year on the subject of new technics of operations or variations of old technics that are described.

It is apparent from the many different types of operations that have been devised, that the principal cause of recurrence lies in the technic and the actual anatomical reconstruction that takes place.

Most recurrent herniæ occur in the direct type and it has generally been found and recorded that the rate of recurrence in direct herniæ is more than twice that of the indirect type. It has been estimated by various authorities that the recurrence rate in direct herniæ is an average of 10 to 20 per cent, even in the hands of experienced operators. For example, Davis of the Massachusetts General Hospital followed up to eighty-eight direct herniæ and found a recurrence rate of 15 per cent.

Therefore, in any consideration of the problem of recurrent hernia, one must include the problem of repair of direct herniæ and large indirect herniæ, which simulate the direct hernia.

The causes of recurrence are generally listed as: (1) failure to remove all of the sac or in some cases, to locate a sac, particularly in the direct type, (2) faulty methods of closure, (3) activity, (4) poor musculature, (5) nerve injury, (6) suture material, (7) chronic lung disease, such as: asthma, bronchiectasis and bronchitis, (8) postoperative complications and (9) wound infection.

In reviewing the recent literature, we find two important changes have taken place. There is a marked tendency toward increasing use of nonabsorbable suture material; chiefly, in the form of silk and cotton and (2) there is a decided increase in the use of the so-called McVay or Cooper's ligament type of repair.

Maier, in 1945, found that there are over seventy modifications of the Bassini type of repair. All these various modifications attempt to strengthen the union between the conjoined tendon and the inguinal ligament.

We now find that with the increasing use of Cooper's ligament procedure, there are many modifications developing and we may expect in the future, various series of cases done by the utilization of the Cooper's ligament.

Among the recent modifications of the McVay type of operation are those uniting the conjoined tendon to the superior pubic ligament. Others employing fascia as suture material, join the conjoined tendon and Cooper's ligament. Also, fascial flaps have been employed and the Bassini and Halsted technics have been used in addition to the Cooper's ligament repair.

---

*Presented before the Postgraduate Course in Gastrointestinal Surgery of the National Gastroenterological Association, Boston, Mass., 27, 28, 29 October 1949.

A recent review of the literature indicates that Swenson and Harkins operated on thirty-seven cases of recurrent inguinal herniæ that were done by fascial graft, and also a McVay type of operation, in which they had no recurrence. It was observed that in all these cases, the so-called relaxing incision was used. The fascial type of repair was done in the first twelve and the McVay type in the last twenty-five cases. In this series of cases, the transversalis and the conjoined tendon were united to Cooper's ligament.

Harkins, et al, on McVay herniæ, found that there were one hundred thirty-one herniæ of several types and in one hundred nine patients they used the McVay type of repair. They used both the Bassini and Halsted modifications, utilizing the superior pubic ligament in all cases. They reported only one recurrence, which was at the internal ring and no serious complications, except for one case of edema of the ankles with question of phlebitis. Silk suture material was used throughout these cases. In all these cases, the so-called relaxing incision was used.

Lich and Samson, in 1943, performed sixty-three Cooper's ligament type of operations and had a percentage of recurrence of 3.1 per cent. Again, they had a further series of twenty-two operations in which Cooper's ligament was employed with no recurrence.

Anson and McVay, in April 1949, reported a series of one hundred cases, fifty-six of which were difficult to repair and twelve of these were recurrences. They have reported no recurrences following their operations. Furthermore, in their series, advanced age was not regarded as a contraindication to repair. No primary wound infections occurred, but there were two cases of abdominal ring repair which later developed sinus tracts, requiring removal of silk mattress sutures.

Anson and McVay called attention to the fact that their work was based on studies including anatomical dissections, that had been made over a period of fourteen years. In their series there were two groups, thirty-five and sixty-five respectively, with the first group five years in duration, but a follow-up that is incomplete. The second group of sixty-five cases shows a follow-up period of ten to twenty-eight months.

Mayo and Keeley described the repair of inguinal herniæ with external oblique fascia, in which they used a McArthur modification. This was used in two hundred twenty-two cases and two hundred eight cases were followed. Pulmonary embolism caused two deaths in their series. In their follow-up, they have proved that the true rate of recurrence in inguinal herniæ can not be determined until five years have elapsed. They have shown that in one hundred fifty-five cases of unilateral herniæ, there is a recurrence rate of 11.5 per cent in five years. Thirty-four cases of bilateral herniæ showed a recurrence rate of 13 per cent in five years. Dividing the time of recurrence into the consecutive years it was found that the recurrence rate was 3.9 per cent for the first year.

Rice and Strichlin have advised a combination of the methods of Bassini, McArthur and McVay, using local fascia and utilizing Cooper's ligament. Rather

than utilizing this procedure only for recurrent herniæ, they have advised using it on the first occasion of a hernia operation. They report a series of forty cases which were repaired without complication.

Zimmerman, in an editorial, "A Critique of the McVay Operation for Inguinal Hernia", expresses several objections to the point of view that utilization of the inguinal ligament is erroneous. He points out that most recurrences take place above the inguinal ligament. Furthermore, he states that any sutures placed in the inguinal ligament must include the distal portions of transversalis fascia and that technically the operation is more difficult. He further points out that the proximity of the femoral veins would be apt to cause a greater incidence of thrombosis.

Also, he suggests the possibility of sutures anchored to the superior pubic ligament may cut through by a process of ischemic necrosis, because of the unyielding quality of the superior pubic ligament. He further expresses doubt that the superior pubic ligament will replace the inguinal ligament in the routine repair of inguinal herniæ.

The importance of a hernia repair that will cut down the incidence of recurrences is very apparent after reviewing the number of hernia cases that were operated on here in a large municipal hospital. In the year 1944 there were five hundred fifty-seven hernia cases admitted to the hospital, and out of this number there were fifty-eight deaths. Of the number of cases admitted, there were two hundred twenty-seven hernia cases operated on with five deaths following operation.

The average age of patients operated on was forty-five and one-half years old; the youngest being five months and the oldest eighty years. In these fifty-eight deaths, that occurred in all these hernia cases, including non-operative and operative cases, there were fifty patients who were over sixty-five years of age. The remaining eight had an average age of fifty-one years. The average age of patients who died following operation, was seventy-four years. Included among the two hundred twenty-seven operations were strangulated herniæ, incarcerated herniæ and various other complicating factors.

Now considering the causes of recurrences as previously noted, a review of one hundred cases of inguinal herniæ operations has been made at the Boston City Hospital, for the purpose of showing the different types of repair that have been used, the complications encountered, and the suture material which has been used. A further observation in these cases was on the use of antibiotics, chiefly in the form of penicillin, which has been used for treatment of minor complications postoperatively. The cases that have been reviewed were taken as consecutive cases as they appeared in the records of admissions in the latter part of 1948 and early 1949.

The average age of these patients operated on in this series, which included a number of children, was forty-eight and one-half years. The different types of repair used show that there were fifty-four Bassini type of repair, twenty-six Cooper's ligament, eight Halsted and twelve Ferguson. The suture material used

was silk in forty-nine cases, cotton in twenty-five cases, catgut in twenty-three cases, wire in two cases and linen in one case. Types of herniæ encountered showed seventy-five indirect herniæ and twenty-five direct cases. Antibiotic medication in the form of penicillin was used in seventeen cases.

It is observed that in these one hundred cases and in the operative record, there was no note made of using the relaxing incision.

There was no mortality due to the operation for herniæ. There was one death in which the patient had a perforated ulcer, which condition was unrelated in any way to the hernia. The number of complications was listed as two cases of deep thrombophlebitis. One of these occurred in a Ferguson repair in which catgut had been used, and in the second, a Bassini type of repair had been used, using catgut for suture material. There were no cases of thrombophlebitis, in those cases where the Cooper's ligament type of repair was used. There was slight bleeding from the wound in one case in which a Cooper's ligament type of repair was done in which silk had been used. There was also one silk sinus which occurred in a Bassini type of repair.

In comparing the Cooper's ligament type of repair with the various other types and also comparing those cases in which silk or cotton was used with those in which catgut was used, there is no apparent disadvantage in the way of comparison, in using Cooper's ligament type of repair and using nonabsorbable material, in the form of silk and cotton.

Now considering the causes of recurrence, it is indicated by our review of one hundred cases in this hospital that without doubt, the technic used in the repair of the hernia is most important in considering the matter of recurrence. In not one case out of one hundred that we reviewed, was there failure to locate a sac. Activity, poor musculature and nerve injury may be eliminated as a cause of recurrence.

It is apparent from a review of the literature that the McVay type of operation, utilizing Cooper's ligament, shows a smaller number of recurrences than previous series using the Bassini, Halsted and McArthur types of repair, and also various fascial types of repair.

Summary

We believe therefore, that on the basis of the recent literature, and a review of one hundred operative cases in this hospital, that the repair of direct and large indirect inguinal herniæ, which more or less simulate the direct type, should be performed by means of the Cooper's ligament repair. This is in order to prevent recurrences.

We also feel that adequate repair of recurrent hernia may be performed by means of the McVay technic, or if one wishes, a modification of this technic in which Cooper's ligament is utilized.

We further believe that there is a considerable advantage in using nonabsorbable suture material in the form of silk or cotton. This is on the basis of a review of recent literature and a review of one hundred cases done here in this hospital,

in which the complications that have occurred in various types are not due to the McVay type of repair, or the use of silk or cotton as suture material.

It is apparent from the series of cases, that the operation using the superior pubic ligament is gaining in popularity. It is to be hoped that further series of cases will be reported in the literature from here on.

Mayo and Keeley have indicated conclusively that we must follow herniæ repairs for a longer period of time, even up to five years, in order to evaluate various types of repairs.

Certainly, this analysis of these cases indicates that the type of repair rather than the complications are the basic causes of recurrence.

We must withhold final judgment on the rate of recurrence in the superior pubic ligament repair until larger series of cases have been followed-up to a period of five years. The present statistics indicate that a comparison between the McVay type of repair and other types of repair may be more favorable to the McVay method.

BIBLIOGRAPHY

Davis, L.: Complications and Sequelæ of the Operation for Inguinal Hernia. J.A.M.A. **67**:480-483.
Maier, R. L.: Results of Silk Technic in Operations for Hernia. Ann. Surg. **113**:312-319, 1941.
Swenson and Harkins: Surgical Treatment of Recurrent Inguinal Hernia with Special Reference to Cooper's Ligament. Surgery. **14**:807-830, 1943.
Harkins, et al.: McVay Herniotomy. Surgery. **12**:364-377.
Lich and Samson: Hernia. L. F. Watson, M.D., 1948 ed., page 284.
Anson and McVay: Surg. Gynec. & Obst. **88**:473-485, (April), 1948.
Mayo and Keeley: Surg. Gynec. & Obst. 603-608, (May), 1949.
Rice and Strichlin: Surg. Gynec. & Obst. **86**: (Feb.), 1948.

ACUTE PERFORATED PEPTIC ULCER*

CHARLES G. SHEDD, M.D., F.A.C.S.†
and
I. SCHWARTZ, M.D.††
Boston, Mass.

This paper is a report on one hundred and forty-two consecutive operations for acute perforated peptic ulcer at the Boston City Hospital. It covers the period from January 1, 1947 to May 1, 1949. The last report from this hospital was published by William R. Morrison[1] in 1935. This study, in our opinion, provides evidence that the improved preoperative care, anesthesia, and postoperative treatment during the past decade has greatly reduced the mortality rate. In addition we should like to re-emphasize some of the important factors as related to the diagnosis and management of this surgical emergency.

Incidence:—During the period from January 1, 1947 to May 1, 1949, there were one hundred forty-two consecutive cases operated upon for perforated peptic ulcer at this hospital with an average yearly incidence of sixty cases.

In addition there were four cases of benign gastroduodenal perforated ulcer which were proven at autopsy and were not operated upon. All of these cases were diagnosed antemortem. These were not included in this series.

In the years 1947 and 1948 there were 19,874 surgical admissions to the five general Surgical Services. (This excludes the Orthopedic, Urologic, Thoracic, Gynecology, and Eye, Ear, Nose and Throat Services.) One hundred twenty of these were operated upon for perforated peptic ulcer, an incidence of 0.6 per cent.

TABLE I
SEASONAL INCIDENCE

Months	Cases	Mortality
Dec., Jan., Feb.	20	0
Mar., Apr., May	26	2
June, July, Aug.	27	1
Sept., Oct., Nov.	47	3
	120	6

Race:—In a large City Hospital, such as ours, the admissions constitute a representative cross-section of all races in the lowest income bracket. Of our one hundred forty-two cases, one hundred thirty-seven were white, four were Negro, and one yellow.

Seasons:—In the two complete years of 1947 and 1948 there was a total of one hundred twenty cases. In the winter, spring and summer seasons, the average incidence was about the same. The greatest incidence in our series was in the fall, in contrast to reports by Luer[2], Collins[3], and DeBakey[4], where the greatest incidence was in the spring. Another report from the Massachusetts General Hospital agrees with our findings.

*Presented before the Postgraduate Course in Gastrointestinal Surgery of the National Gastroenterological Association, Boston, Mass., 27, 28, 29 October 1949.

†Assistant Visiting Surgeon, Second Surgical Service, Boston City Hospital.

††Resident Surgeon, First Surgical Service (Tufts Medical School Teaching Service), Boston City Hospital.

Sex:—There were one hundred thirty-three males and nine females in this series. Five of our deaths were among the males. There was one death in the female group.

Ages:—The majority of the cases (80 per cent) were between thirty and sixty years of age; the forty year age group being the most common. Our youngest patient was twenty; our oldest seventy-six. There was one death in each of the thirty, forty and fifty year age groups, and three deaths in the sixty year age group. The three patients over seventy recovered.

TABLE II
AGES

Ages	Cases	Deaths
20-29	13	0
30-39	32	1
40-49	52	1
50-59	28	1
60-69	14	3
70-79	3	0
Total	142	6

Time of day of Perforation:—The most common time for perforation was between noon and 6:00 P.M. The least frequent time of perforation was between midnight and 6:00 A.M. Similar observations have been reported[2].

Past History:—Half of the cases gave no previous history either suggestive or positive of ulcer. Of the remaining cases, approximately fifty per cent gave a suggestive history and fifty per cent a positive history.

A history was interpreted as being "suggestive" if there were any signs and symptoms consistent with peptic ulcer.

TABLE III
TIME OF DAY OF PERFORATION

Time of Perforation	Cases
Midnight to 6:00 A.M.	28
6:00 A.M. to 12 Noon	33
12 Noon to 6:00 P.M.	44
6:00 P.M. to Midnight	34
Not Stated	3
Total	142

The positive group included those with reperforation, previous hospital admission with a diagnosis of peptic ulcer or a history of positive x-ray diagnosis.

Of the thirty-four positive cases in our series, one-third had symptoms under four years, one-third had symptoms between five and nine years, and one-third ten years or over. The shortest interval prior to perforation was one year and the longest was twenty-five years.

Previous Perforations:—Ten of our patients (7 per cent) gave a history of previous perforation. One case had three previous perforations, nine, eight, and five years prior to his last admission. He recovered uneventfully. Five of the ten cases were alcoholics.

The number of hours from perforation to surgery in this group did not differ from the average of the group as a whole. Apparently, their having had a previous perforation, did not bring them to the hospital any sooner. There was no mortality in this group.

Onset of Present Illness:—Most of our cases (83 per cent) gave a history of "sudden onset of epigastric pain". Seventeen per cent of the patients had a gradual onset of pain.

TABLE IV
ONSET OF PRESENT ILLNESS

	Cases	Deaths
Sudden Onset	118	5
Gradual Onset	24	1
Total	142	6

Signs, Symptoms, Laboratory Aids in the Diagnosis:—It is not our purpose at this time to enter into a thorough discussion of the signs, symptoms and laboratory aids in the diagnosis of ruptured peptic ulcer except to emphasize that eighty per cent of our cases had the triad of: a. sudden onset of pain; b. "board-like" abdomen; c. Pneumoperitoneum.

The white blood cell count in the majority of cases varied between ten and twenty thousand.

Time Elapsed Between Perforation and Surgery:—One hundred seventeen cases (82 per cent) were operated upon within twelve hours of the estimated time of perforation. Of this group only one died; a mortality of less than one per cent.

The mortality rises sharply after twelve hours. From twelve to fifteen hours it is sixteen per cent. From fifteen to eighteen hours it is twenty-five per cent. From eighteen to twenty-one hours it is fifty per cent. Of the six cases that had gone for more than twenty-four hours only one died, a mortality of sixteen and two-thirds per cent.

TABLE V
TIME ELAPSED BETWEEN PERFORATION AND SURGERY

Hours Elapsed	Cases	Deaths	Per Cent Patients	Per Cent Mortality
0-5	38	0	26.8	0
6-8	61	1	43.0	1.6
9-11	18	0	12.7	0
12-14	12	2	8.4	16.6
15-17	4	1	2.8	25.0
18-20	2	1	1.4	50.0
21-22	0	0	—	0
24 and Over	6	1	4.2	16.6
Not Given	1	—	.7	0
Total	142	6	100	4.2

Table V clearly demonstrates the importance of surgery as promptly as possible after perforation, preferably, within twelve hours.

In our opinion the survivals in the twenty-four hour group have spontaneously sealed over the perforation even though the operative note does not always so state.

Preoperative Care:—Our patients are usually seen on our "Accident Admission Floor" at which time a history is taken and physical examination done; a tentative diagnosis arrived at and a decision made as to whether the patient will first be treated in the "Admitting Shock Room" or will go, via x-ray, to the operating room. If the patient is treated in the shock room, adequate shock therapy with oxygen, blood, etc. is carried out. Portable x-ray studies are made of the abdomen and position of the diaphragm. If the patient does not require antishock therapy he is sent through x-ray to get scout films of the abdomen including upright and left lateral decubitus views. From here the patient is sent to the operating room where a complete history is again taken, physical examination carried out, and blood drawn for an emergency hemoglobin, hematocrit, NPN, blood chloride and blood CO_2 determinations. Cells and serum are also drawn for blood typing and grouping in the event the patient will need blood transfusions either before or during the operative procedure. A routine urinalysis is obtained and also a urine specimen sent to the laboratory for diastase determination. It takes approximately one hour for the laboratory results to be reported, during which time a Levine tube is inserted into the patient's stomach for gastric aspiration, using Wangensteen suction. An intravenous infusion of five per cent glucose in saline is started almost simultaneously with the above procedures in which 500,000 units of penicillin are included. If whole blood transfusion is necessary to combat imminent or present shock, it is started just as soon as the blood has been cross-matched for the patient. Only on rare occasions, when no blood is available, is plasma used.

The above mentioned procedures in preparation for surgery and the reestablishment of electrolyte balance are worth a great deal to the outcome of the patient affecting favorably both his operative and postoperative course. We are of the opinion that this hour spent in preparation is *not valuable time lost.*

As soon as all the data is accumulated and studied and a positive or tentative diagnosis made, the patient is given his preoperative medication consisting, usually, of morphine gr. 1/6 and atropine 1/200 intravenously.

TABLE VI
ANESTHESIA

Anesthesia	Cases	Deaths
Spinal	84	2
Combined Anesthesia	49	1
General Inhalation	6	2
Local	2	1
Not Stated	1	0
	142	6

Anesthesia:—Our Anesthesia Service is of the opinion that most patients, whose perforations have occurred within a previous twelve hour period, are usually in favorable condition to receive spinal anesthesia without a supplement. It is felt that a spinal anesthesia is satisfactory first of all because there are few traction reflexes; secondly, it is usually done with a fair amount of speed; thirdly, it is a safer method if the patient is conscious and should have to vomit even in spite of gastric intubation. All patients receive inhalation oxygen during the procedure and

the fluids, started preoperatively, are continued. Occasionally, in a highly nervous individual, supplemental intravenous pentothal is given.

If the patient is in border-line shock condition or has had his perforation for more than twelve hours (and it is usually these patients in whom shock is present or imminent) endotracheal cyclopropane anesthesia is used since it is best tolerated. If necessary for adequate relaxation, the anesthesia is supplemented with intravenous curare.

In this series, one hundred thirty-three patients were given spinal anesthesia alone or in combination with some other supplement such as pentothal, cyclopropane, gas ether or curare. Three deaths occurred in this group. Six of our patients received general endoctracheal anesthesia and in this group, there were two deaths. Two patients were operated upon under local anesthesia and there was one death. It was the opinion of both the Surgical and Anesthesia Services that these deaths were in no way connected with the type of anesthesia used. The latter two types of anesthesia used were reserved for the poorest risk patients.

Location of Ulcer:—There were sixty-two cases (44 per cent) that were stated as being situated on the duodenal side of the pylorus. Fifty-five cases (39 per cent) were located on the gastric side. Twenty cases (14 per cent) were stated as being "pyloric". In five cases the location was not given.

TABLE VII
LOCATION OF ULCER

Location	Cases	Per Cent
Duodenal	62	43.6
Pyloric	20	14.1
Gastric	55	38.8
Not Stated	5	3.5
Total	142	100.0

It was obvious from reading the operative note that in those cases reported as being "pyloric" the exact anatomic location of the perforation was in doubt.

The authors have made careful inquiry amongst the House and Visiting Staff about the accuracy of the anatomic location of perforated ulcers. We have concluded that, when the perforation is situated in close proximity to the pylorus, it is extremely difficult to be certain whether it is gastric or duodenal. In fact the inflammatory reaction about the site of the ulcer makes the location of the pyloric ring nearly impossible. It is our opinion, without statistical proof, that the majority of the ulcers situated in this region are duodenal. DeBakey has made a similar statement[4].

Types of Repair:—One hundred and twenty-five cases (88 per cent) had repair of the perforation made by the use of interrupted seromuscular sutures and either a free or a living omental graft for additional protection. Eight cases had a Graham repair[6]. Four cases had purse string closures and there was one posterior gastric perforation which was closed from within the stomach through a gastrotomy wound. In one case there was an interrupted closure with no omental graft and in

another an omental graft was tacked down over the perforation. In two cases the type of repair was not stated.

TABLE VIII

Types of Repair	Cases
Interrupted Suture Omental Tab	111
Repair Not Stated	2
Purse String	4
Graham Repair	8
Free Omental Graft	14
Gastrostomy and Closure from Within	1
Sutured Over (No Tab)	1
Omental Graft (Tacked Down)	1
Total	142

In all the cases the peritoneal cavity was thoroughly aspirated with special attention given to those areas that are vulnerable to postoperative abscess formation, i.e. supra- and infrahepatic spaces, left subphrenic space, paracolic gutters and pelvis.

Drainage of the peritoneal cavity was done in only one case in this series.

The average operating time was approximately forty-five minutes and almost all the operations were done by the Resident House Staff.

Postoperative Care:—Postoperatively, the patients are followed very closely with pulse, blood pressure and laboratory studies. Wangensteen suction is instituted almost immediately upon return to the ward and is usually maintained from two to four days. Parenteral fluids consisting of glucose, saline, protein hydrolysates and whole blood are given daily during this period as indicated by study of the

TABLE IX

MASON'S GASTRIC REGIME FOR PERFORATED ULCER

First 4 days nothing postoperatively and Wangensteen suction then

First Day—H_2O ounces 1 every hour.
Second Day—H_2O alternating with gruel (with salt and sugar) ounces 2 every hour.
Third Day—H_2O alternating with gruel ounces 3 every hour.
Fourth Day—H_2O ad lib gruel with malted milk ounces four every two hours.
Fifth Day—Same as fourth with 2 crackers with each feeding ounces 6 every 3 hours.
Sixth Day—Same as fifth add cream, soup, egg nog, custard, coddled eggs and soft cooked cereal.
Seventh Day—Add toast and butter, baked potato, ice cream.
Eighth Day—Same as seventh.
Ninth Day—Sippy Diet—Convalescent.
Coffee or tea not to be given unless ordered.
No condiments allowed except moderate amount of salt.
Sugar in moderate amounts.
Bouillon and meat soups to be avoided.

daily fluid losses and electrolyte constituents of the blood. Blood chloride, CO_2 combining power and NPN studies are usually made daily during this initial postoperative period. Penicillin, 100,000 units, every three hours, is given intramuscularly from five to seven days postoperatively. Some of the patients receive five grams of sodium sulfadiazine intravenously during this period.

After the Levine tube is removed, the patient is placed on a "Mason regime of feeding"[7], and this feeding schedule is carried out until the patient is capable

of taking a convalescent Sippy diet which usually takes place on the seventh or eighth day after the removal of the intragastric tube. Beginning on the sixth postoperative day, amphogel and atropine by mouth are added to this regime.

These patients are allowed out of bed on the first postoperative day during which time they are encouraged to walk and take deep breathing exercises. They are not allowed to sit in a chair until at least the fourth postoperative day.

TABLE X

Complication	Cases		Deaths	
1. Pulmonary				
A. Atelectasis	12		1	
B. Empyema	1		0	
C. Bronchitis	2		0	
D. U.R.I.	1		0	
E. Pulmonary Edema	2		0	
F. Pneumonia	1		0	
Total Pulmonary		19		1
2. Delirium Tremens		7		1
3. Peritonitis		4		4
4. Wound Infection		3		0
5. Wound Dehiscence		3		0
6. Evisceration		1		0
7. Cardiac				
A. Arteriosclerotic H. D.	1		0	
B. Coronary	1		1	
C. CVA	1		0	
Total Cardiac		3		1
8. Shock		2		2
9. Sulfadiazine Sensitivity		2		0
10. Subdiaphragmatic Abscess		2		0
11. Pelvic Abscess		1		0
12. Agitated Depression		1		0
13. Phlebothrombosis		1		0
Total		49		9

Most of our Services remove their skin sutures on the seventh to the tenth day, stay sutures on the tenth to the fourteenth day.

The average hospital stay in this group was about fourteen days.

Complications:—Forty-nine cases (34 per cent) in this series had complications.

The largest number of complications were of the pulmonary type, atelectasis being the most prominent in this group. There was one death.

TABLE XI
B.C.H. SERIES

Years	Cases	Deaths	Per Cent Mortality
	Morrison		
1930-1935	200	43	21.0
	Shedd and Schwartz		
1947	65	3	4.61
1948	55	3	5.45
1949 (Jan. 1-May 1)	22	0	0.00
Total	142	6	4.2

The second most common complication was delirium tremens of which there were seven cases with one death, the latter being directly attributable to this complication.

There were three cases of wound dehiscence only one of which eviscerated and came to secondary closure.

The remainder of the complications are summarized in the appended table.

Mortality Rate:—In 1935 Morrison reported an operative mortality rate of 21 per cent in his analysis of two hundred cases of perforated peptic ulcer at the Boston City Hospital for the previous five year period.

DeBakey in 1940 published a comprehensive review comprising a collected series of over 20,000 cases in the world literature covering the decade ending 1939. The operative mortality rate in this series was 23.4 per cent. He concluded that the mortality rate had decreased very slightly during this decade.

TABLE XII

MOST RECENTLY PUBLISHED MORTALITY RATES FOR PERFORATED PEPTIC ULCER (AFTER BARITELL & COLLINS)

Author	Year	No. of Cases	Per Cent Mortality
Baritell, A. L.	1946	88	1.1
Tilton, B. J.	1936	52	2.0
Graham, R. R.	1938	62	3.2
McClure, R. D.	1940	91	7.7
Estes, W. L. and Bennet, B. A.	1944	80	8.7
Black, B. M. and Blackford, R. E.	1945	93	12.0
Barber, R. F. and Madden, J. L.	1943	86	12.8
Hartzell, J. B. and Sorock, M. L.	1939	39	12.8
Marshall, S. F. and Keleher, P. C.	1940	46	13.0
Raw, S. C.	1944	312	14.4
Cohn, R.	1941	300	15.0
Berson, H. L.	1942	151	15.2
Ross, J. C.	1940	175	16.0
Collins, D. C.	1947	36	16.7
Paletta, F. X. and Hill, W. R.	1943	83	16.9
DeBakey, M. and Odom, C. B.	1940	211	17.3
Ross, A. and LaTourneau, G.	1939	220	17.7
Donald, D. C. and Barkett, S. M.	1942	116	18.5
Meade, R. H.	1943	68	19.1
Timoney, F. X.	1943	246	19.5
Griswold, A. R. and Antoncic	1941	102	19.6
Fallis, L. S.	1938	100	20.0
McCreery, J. A.	1938	170	20.5
Eliason, E. L. and Thigpen, G. M.	1938	70	21.4
Sangster, A. H.	1939	100	23.0
O'Donohue, J. B. and Jacobs, M.	1942	200	24.5
McCabe, E. J. and Mersheimer, W.	1943	87	25.2
Martz, H. and Foote, M. H.	1940	50	26.0
Parker, E. F.	1941	52	27.0
Davidon, T. C. and Rudder, F. F.	1940	155	28.0
Thompson, H. L.	1939	424	28.7
Hartzell, J. B. and Sorock, M. L.	1939	234	28.9
Reed, J. C.	1939	100	30.0
Shedd, C. G. and Schwartz, I.	1949	142	4.2

In 1942 Ulfelder and Allen reported on 324 cases from the Massachusetts General Hospital covering the period from 1916 to 1940. Their general mortality for this period was 27.1 per cent. They demonstrated that the mortality, considered by five year periods during this study, showed no significant change.

The operative mortality of our series is 4.2 per cent, a decided drop in comparison with the above reports. Further comparison of our mortality with the other more recent reports in the literature is given in Table XII.

Summary and Conclusion

A statistical analysis of one hundred and forty-two consecutively operated upon cases with a diagnosis of perforated peptic ulcer from January 1, 1947 to May 1, 1949 is made. The mortality rate of this group is 4.2 per cent. A decline of 17 per cent from a previously reported series from this hospital in 1935 is noted. We believe that the factors responsible for this lowered mortality rate are improved pre- and postoperative care, anesthesia, and early operation (within twelve hours of perforation).

REFERENCES

1. Morrison, William R.: Two Hundred Acute Perforated Ulcers of the Stomach and Duodenum from the Boston City Hospital. New England J. Med. **213**:447, 1935.
2. Luer, Carlyle A.: Acute Perforations of Stomach and Small Bowel Ulcerations. Surgery. **25**:404, 1949.
3. Collins, Donald C.: Modern Management of Acute Perforated Gastroduodenal Ulcers. Am. J. Surg. **77**:684, 1949.
4. DeBakey, Michael: Acute Gastroduodenal Ulceration. A Statistical Analysis and Review of the Literature. Surgery. **8**:852, 1028, 1940.
5. Ulfelder, Howard and Allen, A. W.: Acute Perforations of Ulcers of the Stomach and Duodenum. New England J. Med. **227**:780, 1942.
6. Graham, R. R. and Tovee, E. B.: Treatment of Perforated Duodenal Ulcers. Surgery. **17**:704, 1945.
7. Mason, Robert L. and Zintell, Harold A.: Preoperative and Postoperative Treatment. Second Edition, Philadelphia, W. B. Saunders Company, 408, 1946.
8. Baritell, A. L.: Perforated Gastroduodenal Ulcer. Surgery. **21**, **24**, 1947.

SURGICAL ASPECTS OF DIVERTICULITIS OF THE SIGMOID*

J. EDWARD FLYNN, M.D., F.A.C.S.

Boston, Mass.

Surgery in the management of diverticulitis of the sigmoid is limited mainly to the treatment of certain complications, namely perforation with a localized abscess or general peritonitis, obstruction and fistula. A thorough investigation and frequent study, by the internist and surgeon, is important in making a determined effort to avoid operation. However, it is unreasonable and dangerous to persist in a medical treatment after development of the above mentioned complications. It is frequently impossible to exclude carcinoma on clinical investigation, and exploration for this reason is necessary. Since the advent of modern chemotherapy, surgery of the colon has made great progress, especially in decreasing the immediate mortality.

This study was made of patients whose diverticulitis involved the sigmoid only, or the sigmoid together with a portion of the descending colon and who were treated surgically. One hundred cases which were treated at the Boston City Hospital since the advent of modern chemotherapy, and ten cases which were personally studied at the Veterans Administration Hospital, West Roxbury, are included in this investigation.

Incidence:—The exact incidence of diverticulosis is unknown. The number of patients with diverticulosis in whom symptoms, due to inflammatory changes in the diverticula, will develop, is unknown. It is not known in what proportion of patients with diverticulitis, operation will be necessary.

Diverticulosis of the colon is rare under forty years of age. It is estimated that over five per cent of people more than forty years of age have diverticulosis. Pemberton[1] reports that of more than 47,000 rœntgenologic examinations, made at the Mayo Clinic over a five year period, diverticulosis was discovered in 8.5 per cent. In this same period the diagnosis of diverticulitis of the sigmoid was made in 600 cases, which represents 15 per cent of the cases of diverticulosis. Of the 600 cases of diverticulitis, operation was performed in 144 cases, or 24 per cent.

Abell[2] has estimated that 10 to 20 per cent, and Brown and Marcley[3] that 12 to 16 per cent, of patients with diverticulosis ultimately will have diverticulitis.

The 100 cases operated upon at the Boston City Hospital were encountered from 1942 to 1949. Over this same period 438 cases of diverticulitis were treated at this hospital, about 22 per cent requiring surgical treatment. In our series about one out of every five cases of diverticulitis required surgery.

Etiology:—The etiology of diverticula formation is not certain, but McGrath[4], as the result of combined anatomical and experimental investigation, came to the following conclusions: No single factor explains the origin of the ordinary form

*Presented before the Postgraduate Course in Gastrointestinal Surgery of the National Gastroenterological Association, Boston, Mass., 27, 28, 29 October 1949.

of diverticula. As in the case of an aneurism or an ordinary hernia the fundamental factors are insufficient resistance of the wall and increased pressure from within. The cause of the weakening of the wall is undecided. It is probably not a congenital defect, as diverticulosis is very rare before middle age. Spriggs and Marxer[5] suggested that an inflammatory process, the result of infection, may play an important part, but Mailer[6] could find no evidence in support of this in his material. It appears most probable that the weakness is degenerative in character, due to loss of tone and elasticity of muscle which is characteristic of the degenerative period of life. Chronic constipation can hardly play an important part, otherwise the condition would be more common in women than in men, whereas the reverse is the case. During peristalsis a wave of relaxation precedes the wave of contraction. It has been suggested that a relaxed segment may be caught between two contracting segments, and a herniation started in this way. Such protrusions have been observed at operation. Possibly, neuromuscular unbalance may be responsible[7].

TABLE I

Symptoms and Signs	Cases	Per cent
Inflammation – Tenderness Fever Leucocytosis	98	89
Abdominal Pain	82	74
Constipation	74	67
Vomiting	56	59
Diarrhea	45	40
Blood in Stool	22	20
Mucus in Feces	19	17
Weight loss	9	8

Age and Sex:—In our series the youngest male was twenty-nine years, and the youngest female thirty-five years of age; the oldest male was eighty years and the oldest female eighty-two years of age. The mean age was fifty-seven years at the time of the operation. The ratio of males to females was two to one.

Age and Time of Operation:—In this series, diverticulitis, in many patients, was severe from the onset of symptoms, and many required operation relatively soon after the onset of symptoms. Thirty-eight per cent of patients were operated on within one month and fifty-seven per cent within six months of the onset of symptoms. That more of the older patients were operated upon sooner after the onset of symptoms than were the younger patients is in keeping with the reports of others. Twenty-nine per cent of patients in their forties or less were operated on within six months of the first symptoms; forty-two per cent of those in their fifties, and fifty per cent of those in their sixties or more.

Symptoms and Signs:—The incidence of symptoms and signs are shown in Table I. The symptoms in the order of their frequency were tenderness, fever and

leucocytosis, abdominal pain, constipation, vomiting, diarrhea, blood in stools, mucus in feces and weight loss.

Sigmoidoscopy is of great value in the diagnosis of diverticulitis of the sigmoid. The findings which are suggestive of diverticulitis are diverticula, edema of the mucous membrane, constriction of the lumen, fixation of the bowel, angulation and an extraluminal mass. Of the seventy-three patients subjected to sigmoidoscopy, findings suggestive of diverticulitis were seen in fifty-seven per cent.

X-ray examination after barium enema is also a great aid in diagnosis. This examination was performed on seventy-four patients. Fistula of the sigmoid was diagnosed in nine per cent. An obstructing lesion of questionable malignancy was found in six per cent, and obstructing lesion was seen in twenty-six per cent, and a diagnosis of diverticulitis, diverticulosis or both was made in fifty-nine per cent.

TABLE II

Incidence of Complications (Additional Signs)

	Cases	Per cent
1. *Perforation*		
Mass	74	67
Abdominal	55	50
Pelvic	19	17
General Peritonitis	18	16
2. *Intestinal Obstruction*		
Partial	45	40
Complete	5	4
Total	50	44
3. *Fistula*		
Sigmoid Cutaneous	19	17
Sigmoid Vesical	6	5
Sigmoid Enteric	4	3
Total	29	25

Relationship of Diverticulitis to Carcinoma:—Earlier writers suggested that carcinoma may develop in conjunction with diverticulitis[8], and that the chronic irritation may lead to production of carcinoma. However, it is now generally agreed that carcinoma is no more likely to develop upon diverticulitis than it is to develop in a bowel not so involved. Rankin and Brown[9] state that in 227 cases of diverticulitis, carcinoma was found in four and that in 679 cases of carcinoma, diverticulitis was found in only four cases. In 110 cases of diverticulitis in our series, malignancy was encountered in five cases. In one case carcinoma involved the sigmoid, in another carcinoma involved the transverse colon. In the other three cases the malignancy was found outside of the gastrointestinal tract—carcinoma of the bladder, carcinoma of the breast and retroperitoneal sarcoma. This finding

would indicate that malignancy had no more tendency to occur in a bowel involved with diverticulitis than it has to occur elsewhere.

Clinically and by the gross appearance at operation, it may be impossible to differentiate diverticulitis from carcinoma. On clinical examination, twenty-five per cent of our cases of diverticulitis could not be differentiated from carcinoma.

Incidence of Complications:—The incidence of complications of diverticulitis is shown in Table II. Perforation with a localized mass was the commonest complication and was found in sixty-seven per cent. Perforation with general peritonitis was relatively high in our series, sixteen per cent, which is characteristic of the stage in any disease which many patients have on entering a Municipal Hospital. Intestinal obstruction was found in forty-four per cent and fistula formation in twenty-five per cent.

Mortality:—Operated cases for diverticulitis may be classified into three groups—general peritonitis, abdominal and pelvic abscess with or without obstruction and fistula formation. Mortality rate is better indicated by stating statistics for each group, rather than giving one overall figure. Mortality with general peritonitis was fifty per cent, for abdominal and pelvic abscess with or without obstruction five per cent and with fistula formation seven per cent.

Preoperative Treatment:—The preoperative treatment is similar to that for any colon lesion. The patient should be hospitalized for three to five days or longer before operation. The general principles in the treatment are: to decompress and cleanse the large bowel; to combat loss of blood and to establish and maintain protein balance by blood transfusions; to combat dehydration by intravenous injection of saline and glucose solutions; to establish and maintain concentration of vitamins, especially Vitamins C and K; to combat potential infection by chemotherapy.

Chemotherapy has proven to be of great value in the preoperative treatment. It has been shown that the commonest indication for surgery is a perforation of the diverticulitis with abscess formation and this type of case may be difficult to differentiate from carcinoma. In six of eight personally treated cases, with abscess formation, the mass resolved clinically with chemotherapy, and this fact makes the differential diagnosis between carcinoma and diverticulitis easier at operation. One hundred thousand units of penicillin are given every three hours and half a gram of streptomycin is given four times a day. The streptomycin is continued as long as the patient improves. If no improvement is noted in the patient, the streptomycin is omitted in three days. The average time required for a mass to disappear, with penicillin and streptomycin therapy, was sixteen days, in which cases the chemotherapy was continued until transverse colostomy was performed. Succinyl sulfathiazole (sulfasuxidine) is given for three to five days before transverse colostomy, in doses of twelve to fifteen grams daily by mouth.

Miscellaneous Operation:—Various operations have been performed at the Boston City Hospital as in other hospitals for diverticulitis. Patients given the same operation were grouped together and results were evaluated as to immediate

mortality and ultimate results. It is a fact that when the inflammatory lesion is not resected, recurrence of the diverticulitis is always a possibility.

The various surgical procedures presented were all carried out at the Boston City Hospital. The number of cases submitted to some procedures were small, yet give some evidence as to the ultimate outcome. Drainage of pelvic abscess, drainage for general peritonitis and closure of sigmoid perforation without colostomy were followed by poor results. Colostomy with subsequent excision of fistula and later closure of colostomy without resection of sigmoid gave unsatisfactory results. Colostomy, partial colectomy and ileosigmoidoscopy were performed in two cases where inflammation developed in diverticula proximal to the sigmoid and subsequent to diverticulitis of the sigmoid. Closure of sigmoid perforation with colostomy gave temporary good results, but gave poor results in two-thirds of the cases when the colostomy was closed without resection of the sigmoid. Table III shows the number of cases and results with the above surgical procedures.

TABLE III

Miscellaneous Operations

Operations	Cases	Results		Mortality	
		Good	Bad	Cases	Per cent
Drainage of Pelvic Abscess	6	2	4	1	16
Drainage of General Peritonitis	14	5	9	7	50
Colostomy, Partial Colectomy, Ileosigmoidostomy	2	2	0	0	0
Colostomy, Excision of Fistula only, Closure of Colostomy	6	2	4	2	33
Closure of Sigmoid Perforation Without Colostomy	2	0	2	1	50
Closure of Sigmoid Perforation With colostomy	6	2	4	0	0

Common Surgical Procedures and Results:—Colostomy, for perforated diverticulitis with local abscess formation, was followed by immediate good effects in most cases and by ultimately good results when resection of the involved segment was performed. For perforation with general peritonitis, proximal colostomy is the treatment of choice when the condition of the patient can stand the procedure. However, with general peritonitis as a complication, the mortality is high, regardless of the procedure. Colostomy, proximal to the segment involved by the diverticulitis, is followed by subsidence of inflammatory reaction in six months in most patients. However, in one case, the reaction had not subsided in twenty-two months. With a proximal colostomy, for the treatment of diverticulitis, there is no certain way to determine if the colostomy can be closed without recurrence of the disease. Resection of the involved sigmoid should be performed in all cases before closure of the colostomy; unless clinical examination, sigmoidoscopic examination

and barium enema show no evidence of the disease and, even in such cases subsequent attacks of diverticulitis may occur. Pemberton reports that, in thirty-one patients treated with proximal colostomy and later closure of the colostomy without resection of the disease, satisfactory outcome was achieved in less than one-third of the patients. In our series at the Boston City Hospital, nine patients with colostomy were subjected to closure of the colostomy without resection of the sigmoid with a recurrence of the disease in six cases.

Primary exteriorization may be performed when the reaction is small. However, primary exteriorization should not be attempted when the peridiverticulitis is extensive, as the risk is too great. The mortality, in our series, with primary exteriorization, was six per cent.

A preliminary transverse colostomy and subsequent exteriorization is a procedure which should be performed when edema of the colon proximal and distal to the diverticulitis would render end-to-end anastomosis hazardous, at the time of resection. In our series, eighteen patients were treated in this fashion with no mortality.

A preliminary colostomy with subsequent resection and end-to-end anastomosis is the surgical treatment of choice for diverticulitis. In most cases clinical evidence, barium enema and sigmoidoscopic examination will reveal the process quiescent enough, six months after colostomy, to permit resection and end-to-end anastomosis. If clinical examinations, x-ray examinations, and sigmoidoscopic examination show that the inflammatory process has not subsided in six months, resection should be delayed until the inflammatory process subsides. In our series of twenty-one cases treated with proximal colostomy, a later resection of the sigmoid and end-to-end anastomosis, there were no deaths.

A primary resection, with end-to-end anastomosis and with no proximal colostomy, is a dangerous procedure which will be accompanied by a relatively high mortality. This procedure should be reserved only for a small localized lesion when there has been adequate preoperative preparation of the colon with antibiotics. In five cases treated by this procedure, in our series, there was one death.

A resection of the sigmoid with end-to-end anastomosis and with a proximal colostomy may be performed rarely, and should be reserved for small lesions of the sigmoid with slight inflammatory reaction. Seven of our cases were subjected to this procedure with no mortality.

For cutaneous, bladder, and enteric fistulæ, eight cases were treated by a preliminary colostomy, later repair of the fistula and resection of the sigmoid, and subsequent closure of the colostomy. There was no mortality. Table IV shows the number of cases, results and mortality with the more common surgical procedures.

Treatment Recommended:—Stage I. A right upper paramedian incision is made. Exploration of liver, mesentery and sigmoid is made to differentiate diverticulitis from carcinoma, if there is no general peritonitis. A right transverse colostomy is performed for obstruction, fistula, perforation with local abscess formation and for perforation with general peritonitis when the patient's condition will

withstand this procedure. A simple loop colostomy has provided adequate diversion of the fecal stream in our patients. We have performed a Wangensteen type of colostomy, which provides a more complete diversion of the fecal stream, in some of our patients.

Stage II. Six months later, after clinical examination, barium enema and sigmoidoscopic examination show that the inflammatory process has subsided, the sigmoid is resected. An end-to-end anastomosis is usually performed. However if the bowel proximal and distal to the resected sigmoid is edematous, the two loops are exteriorized.

TABLE IV

Surgical Procedures—Results and Mortality Rate

Surgical Procedures	Patients	Results		Deaths	Per cent
		Good	Bad		
Colostomy for Local Abscess	22	20	2	1	5
Colostomy for General Peritonitis	4	2	2	2	50
Colostomy, Subsequent Closure, Without Resection	9	3	6	0	0
Colostomy, Subsequent Exteriorization	18	16	2	0	0
Primary Exteriorization	16	13	3	1	6
Colostomy, Subsequent Resection, End-To-End Anastomosis	21	19	2	0	0
Primary Resection, End-To-End Anastomosis, no Colostomy	5	4	1	1	20
Primary Resection, End-To-End Anastomosis and Colostomy	7	6	1	0	0
Colostomy, Repair Fistula, Resect Sigmoid, Close Colostomy	8	7	1	0	0

A fistula is corrected previous to resection of the sigmoid and the sigmoid is resected at this operation or later if the patient's general condition contraindicates resection. We believe that the patient with a fistula should have a resection of the sigmoid before the colostomy is closed, because otherwise the original disease remains and the possibility of recurrence in at least two-thirds is present.

Stage III. Two months after resection, the colostomy is closed; when clinical evidence, barium enema and sigmoidoscopy are within normal limits.

Comment

Progress in surgery of diverticulitis, since the advent of chemotherapy, has not developed as rapidly as other gastrointestinal surgery. Team work between the internist and surgeon has increased the indications for surgery in peptic ulcer, decreased the complication of peptic ulcer and has decreased the mortality with peptic ulcer.

Previous to antibiotics, colonic surgery, even with technically errorless technic, could not be performed with assurance that fatal peritonitis would not occur. However, since the introduction of chemotherapy, lesions of the colon and rectum have survived uncomplicated resection without much concern.

The indications for surgery with gastric ulcer are well understood and need no review. Generally, the indications for surgery with duodenal ulcer, without complication, are failure of medical treatment.

The indications for surgery with diverticulitis of the sigmoid now are complications of this disease—obstruction, fistula formation, perforation with local abscess formations or general peritonitis. We now have a medical and surgical team studying these patients before complications occur. The main difficulty is that many of these patients, particularly the older age group, do not present themselves for treatment until complications have developed. Patients with diverticula should be examined every six months or earlier if intestinal symptoms occur because about fifteen per cent of those with diverticula will develop diverticulitis. Patients with uncomplicated diverticulitis should be followed closely during the presence of symptoms. The treatment of uncomplicated diverticulitis of the sigmoid is conservative, as is the treatment of chronic duodenal ulcer. The treatment consists of rest, low residue diet, antibiotics and oil laxatives as indicated. However, if the diverticulitis does not respond to a medical régime over a six month adequate treatment, surgery may be indicated. Two or three recurrent attacks of uncomplicated diverticulitis over the period of one year, which can be controlled with difficulty, probably should be subjected to surgery.

Previous to antibiotics the mortality with surgery in diverticulitis of the sigmoid was fifteen per cent. With a reduction in mortality to five per cent, since the advent of antibiotics, the suggestion that operation should be advised for uncomplicated but uncontrolled diverticulitis must be entertained. The surgical mortality could probably be reduced if patients with uncontrolled diverticulitis were operated upon, and a greater number of resections with primary anastomosis could be performed. Medical treatment of uncontrolled diverticulitis is associated with great uncertainty as compared to a cure with removal of the diseased bowel.

Summary

The indications for surgery with diverticulitis of the sigmoid at present are limited to complications of this disease—obstruction, fistula and perforation. Perforation with general peritonitis in a municipal hospital seems to be greater in incidence than in private hospitals.

A proximal colostomy should be performed with obstruction, fistula and perforation with abscess formation, and for perforation with general peritonitis when the condition of the patient will permit this procedure.

Results following closure of the colostomy without resection of the involved bowel are generally unsatisfactory, so that resection should be performed in all cases unless absolute proof of complete subsidence of the inflammatory process can be proved.

The commonest complication of diverticulitis is local abscess formation with peridiverticulitis. After an interval of six months with a proximal colostomy, a resection of the diseased bowel can usually be performed with end-to-end anastomosis. However, if there is edema of the bowel proximal and distal to the resected segment, exteriorization of the diseased bowel should be performed. The colostomy is usually closed two months after the resection, if clinical examination, barium enema and sigmoidoscopy are within normal limits.

With the risk of operations reduced by chemotherapy, the scope for surgery, particularly in the uncontrolled uncomplicated diverticulitis, should probably be broadened.

REFERENCES

1. Pemberton, J. de J., Black, B. M., Maino, C. R.: Progress in Surgical Management of Diverticulitis of the Sigmoid Colon. Surg., Gynec. & Obst. **85**:523-534, 1947.
2. Abell, I.: Diagnosis and Treatment of Diverticulitis and Diverticulosis. Surg., Gynec. & Obst. **60**:370-378, 1935.
3. Brown, P. W. and Marcley, D. M. J.: Prognosis of Diverticulitis and Diverticulosis of the Colon. J.A.M.A. **109**:1328-1333, 1937.
4. McGrath, B. F.: Intestinal Diverticula, Their Etiology and Pathogenesis. Surg., Gynec. & Obst. **15**:429, 1912.
5. Spriggs, E. I. and Marxer, O. A.: Intestinal Diverticula. Quart. J. Med. **19**:1-34, 1925.
6. Mailer, R.: Observations on Diverticula of the Colon; Pathological and Clinical Study. Lancet. **2**:51-57, 1928.
7. Boyd, W.: Surgical Pathology, 6th Edition. W. B. Saunders Co., Phila., Pa., 1947.
8. Mayo, W. J.: Diverticulitis of the Large Intestine. J.A.M.A. **69**:781, 1917.
9. Rankin, F. W. and Brown, P. W.: Diverticulitis of the Colon. Surg., Gynec. & Obst. **50**:836-847, 1930.

DIAPHRAGMATIC HERNIA WITH REPORT OF A CASE

ROY UPHAM, M.D., F.A.C.S., F.I.C.S.
New York, N. Y.

Diaphragmatic hernia is one of the unexpected findings in an analysis of symptoms characterized by upper abdominal pain. While it was first diagnosed several hundred years ago by autopsy, it is only within the last three or four decades that the diagnosis is being clinically established, and diaphragmatic hernia is revealed with increasing frequency. The condition was considered uncommon in the past, but with a better understood symptomatic picture, routine rœntgen search in every gastrointestinal tract study, and the fact that the clinician is constantly on the watch for it, the diagnosis of diaphragmatic hernia is being made with greater frequency. For example, up to 1912 only 15 cases had been reported as having been correctly diagnosed, whereas at the present time thousands of cases have been reported in the literature.

Because many cases occurred over the years without clinical symptoms being ascribed to the condition, it is essential that thought be devoted to the herniæ that give rise to symptoms and to try and establish the history-symptom complex and the methods to be employed in establishing the diagnosis.

This study of the subject is prompted by the unusual history of a diaphragmatic hernia in a patient in whom three-fourths of the stomach was above the diaphragm. A second feature is the fact that a large part of the stomach was above the liver, extending well to the right side of the thorax. Finally, the stomach approached the inversion type. Apparently few cases of this type have been reported.

Case Report

Miss V. C., age 62 years, had some attacks of abdominal distress at the time of her menstrual period during early life. There was no severe abdominal pain, nausea, or vomiting until she was 35 when there was an acute attack of nausea and vomiting which lasted for several days. During the next 23 years there were intermittent attacks of nausea, but no pain.

It was not until the patient was 58 years of age that characteristic attacks of pain in the upper right quadrant of the abdomen occurred; these usually came on about 11.00 A.M. and continued during most of the day, and late in the day there was an attack of vomiting. The pain radiated up under the sternum and into the back. There was some distention in the epigastric area. The pain was usually relieved by vomiting. Between attacks the patient was entirely free from pain. During the first two years the intervals between attacks were about eight months, but in the last six months they were reduced to six weeks. Between attacks her appetite was poor, but in spite of this she weighed 170 pounds, although she was only 5 feet, 3 inches in height. There was some nausea after eating, but never any dysphagia and, apart from the attacks, there was no pain. The only distress reported was that due to distention.

Physical Examination

Skin:—Normal.

Eyes:—Reacted normally to light and distance. No nystagmus.

Mouth:—Complete upper and lower dentures. Tongue showed a thin coating. No tremor. No pigmentation. Tonsils normal.

Neck:—No goiter or enlarged glands.

Heart:—Apex beat in normal position. No murmur. Pulse 72; regular.

Lungs:—Normal.

Abdomen:—Abdominal wall fat. No umbilical hernia, enlarged veins nor enlarged glands. Upper border of liver in normal position; lower border normal. Gallbladder tender. Pancreas and spleen normal. Appendectomy scar. Both kidneys normal. No tumor or tenderness along the course of the colon. No mass in the abdomen. No hernia, right or left, inguinal or femoral.

Rectum:—No masses felt. Digital examination reveals internal hemorrhoids. Sphincter normal.

Neurological:—Knee-jerks normal. No abnormal reflexes elicited.

Lower Extremities:—Varicose veins present. No edema. Brachials sclerosed.

Blood Pressure:—110 systolic; 70 diastolic.

Laboratory Data

Seven stools were negative for blood on a meat-free diet.

Hematological Examination:—Red blood cells, 4,630,000. Hemoglobin, 85 per cent. White blood cells, 6,250.

Urine:—Negative except for a slight trace of albumin.

Fractional Examination:—after an alcohol meal, showed a total acidity of 47 with a free hydrochloric acid of 15.

Blood Wassermann:—Negative.

Sedimentation Rate:—21.

Roentgenologic Examination

This disclosed the stomach herniated into the thorax, extending over to the right side in an inverted position, occupying the area above the liver.

In a study of diaphragmatic hernia, a consideration of the development of the diaphragm leads to a better understanding of the various locations where the hernia may occur. In the posterior region of the diaphragm, which is covered by the pleuroperitoneal membrane, is the foramen of Bochdalek, which is the most infrequent site of a hernia. At the anterior surface of the thoracic cavity, in the region of the ensiform, are two openings, the foramina of Morgagni, which are located on each side of the sternum and are potentially weak spots in the diaphragm. The opening for the passage of the esophagus through the diaphragm is the most frequent site of hernia. Incomplete development of this hiatus may permit the herniation of the stomach through it.

Failure of embryologic development of any segment of the diaphragm may result in a complete absence of half of the diaphragm, or small openings may occur anywhere in its substance.

There are numerous classifications of diaphragmatic hernia. Akerlund, who has devoted much thought to the subject, has presented the simplest classification, but it contains an error, even in its simplicity, because he has included the congenital short esophagus. The congenital short esophagus produces a thoracic stomach, but since the organ is never below the diaphragm, it cannot be called diaphragmatic hernia. Akerlund divides his classification into three categories: In the first, the esophagus is too short and pulls the cardia up through the diaphragm. In the second, the cardia is in place, but the fundus has forced its way beside the esophagus. In the third, both the cardia and adjacent region of the stomach are pressed upward, even though the esophagus is normal.

While the classification of Harrington appears more complex, it is the most satisfactory approach to a study of the subject:

I. Diaphragmatic hernia.
  A. Nontraumatic lesions:
    1. Congenital:
      a. Pleuroperitoneal (foramen of Bochdalek)
      b. Esophageal hiatus (congenital type):
        (1) Paraesophageal
        (2) Esophageal hiatal
      c. Short esophagus:
        (1) Congenital short esophagus
      d. Anterior substernal (foramen of Morgagni-Larrey's spaces)
      e. Gaps in or partial absence of the diaphragm (posterior portion of the diaphragm)
      f. Complete absence of hemidiaphragm
    2. Acquired:
      a. Esophageal hiatus
        (1) Pulsion type:
          (a) Similar to paraesophageal
          (b) Similar to esophageal hiatal
      b. Short esophagus
        (2) (Not congenital) ulceration and cicatricial contraction which draws the stomach above the diaphragm
      c. Through regions of fusion of the anlage of the diaphragm
      d. At sites named in the congenital type
  B. Traumatic:
    1. Indirect injury:
      a. Anywhere in diaphragm
      b. Points of embryologic fusion
      c. Dome and posterior half of the diaphragm
    2. Direct injury:
      a. Any point in the diaphragm

3. Result of inflammatory necrosis:
   a. Subdiaphragmatic abscess or drainage tubes
   b. Usually posterior portion of the diaphragm

II. Eventration

It would seem that a further distinction between a short esophagus and a shortened esophagus should be made.

As a rule, hiatus herniæ are genuine; that is, they are herniæ with true sacs.

Reports of the incidence of diaphragmatic hernia vary considerably; ranging from 1 per cent to 8 per cent. Branwood reports 15 cases in 300 consecutive examinations. Undoubtedly, the figures vary in large groups of cases investigated.

As the discussion of the etiology will indicate, diaphragmatic hernia and, in particular, hiatus hernia, occurs more frequently in the older age groups. This does not invalidate the fact that many cases are reported in the newborn. The frequent occurrence of the condition in the latter is due to congenital defects of the diaphragm. Diaphragmatic hernia in infancy is discovered shortly after birth, usually in general hospitals and pediatric divisions, and is not of general interest to the gastroenterologist. Where the condition occurs later in life there may have been a congenital enlargement of the normal openings in the diaphragm. The deterioration of the elastic tissue surrounding the openings in advancing years, and the increased deposition of fat in the tissues allows for the stretching of the openings under abnormal increase of intraabdominal pressure and, as a consequence, herniation results.

Etiology

The cause of diaphragmatic hernia is a large aperture in the diaphragm which may be congenital or traumatic, or potentially a large aperture in one of the hiatal openings, in addition to a weakness of the musculature.

In considering the etiology, the classification of traumatic herniæ merits attention. These may arise from actual injury of the diaphragm by penetrating wounds, rifle bullets, or sword thrusts. Some of the earlier cases reported were of this character. With the advent of the automobile and the extreme crushing injuries which occur in automobile accidents there has been an increasing number of traumatic hernia. Trauma may produce an immediate hernia, or there may be a prolonged interval of progressive degeneration, or a weakened area in the diaphragm which, favored by some subsequent element of increased intraabdominal pressure, produces a hernia long after the original injury.

This category also includes the degenerative changes which can occur in the diaphragm from infection and other causes which produce areas of weakness in the diaphragm, allowing subsequent separation of its fibres.

In congenital diaphragmatic hernia there may be complete or partial absence of the diaphragm.

The cause of cases occurring in later life is, first, abnormally large openings in the diaphragm which are further weakened by the disappearance of the elastic tissue about the openings, and, secondly, fatty changes coincident with advancing years.

Mention should also be made of a history of sudden strain, repeated pregnancies, the presence of a large abdominal tumor, severe and prolonged attacks of coughing, or any factor producing increased intraabdominal pressure, such as tight lacing or abdominal constriction of any type.

A further etiologic factor as far as hiatus hernia is concerned is cholecystitis or other abdominal disease leading to a reflex contraction of the vagus, which, in turn, causes a shortening of the longitudinal fibres of the esophagus, thus producing contraction and drawing the stomach into the hiatus opening. The fact that many of these factors are far more frequent in the female than in the male sex accounts for the finding of diaphragmatic hernia about seven times as frequently in the female.

Injuries incident to World War I further stimulated the diagnosis and treatment of the condition.

Protrusion of an abdominal organ into the thoracic cavity through any of the openings, either natural or artificial, may be defined as a diaphragmatic hernia. By far the most common site of diaphragmatic hernia is the esophageal opening: 80 per cent occur through this opening, about 10 per cent through the foramina of Morgagni, 7 per cent through the foramen of Bochdalek, and 3 per cent through the costophrenic space.

Diagnosis

From a diagnostic standpoint, diaphragmatic hernia is interesting because it occurs as a masquerader and mimics many symptoms of other conditions in the upper abdomen. Prior to the advent of the rœntgen ray, diaphragmatic hernia was considered a medical and surgical rarity. The rœntgen ray is the means whereby the condition is most frequently diagnosed, and it certainly deserves all credit for the early studies which developed the story and romance of this diagnosis.

Truesdale reported over 60 varieties of diaphragmatic hernia, and when we realize that almost every organ in the abdomen, except the bladder, has been found in a diaphragmatic hernia, it is increasingly evident that the general symptom-complex may vary according to the organs involved. However, cases can be broadly divided into those presenting disturbances of the gastrointestinal tract, particularly the stomach, and those involving the thoracic organs, either by pressure of the abnormal contents within the thorax or through constitutional conditions. It can be readily understood how bizarre the symptoms can be when the organ involved may be, as in the case herein reported, a stomach almost entirely within the thorax with gastric symptoms, as compared with the ones that may occur in the foramina of Morgagni, which may involve only pinching of the omentum in the hernia, and those occurring in the foramen of Bochdalek involving only the colon, with resultant constriction of the narrowed neck of the hernia, thus giving rise to symptoms of intestinal obstruction.

Probably the most reliable symptom is the epigastric pain which occurs on lying down or on exertion and intensified by any form of increasing intraabdominal pressure. It may come on after the patient has been lying down for some hours at night, forcing him to sit up in bed, or even to stand erect. Some of these herniæ may be of the sliding variety and return to the abdominal cavity when the patient assumes the latter posture. Others may empty their contents into the lower section of the organ beneath the hernial opening in the diaphragm.

Another symptom is gastric pain which is increased by coughing or sneezing. While this pain may be confused with that of ulcer, it is not regular as to time and

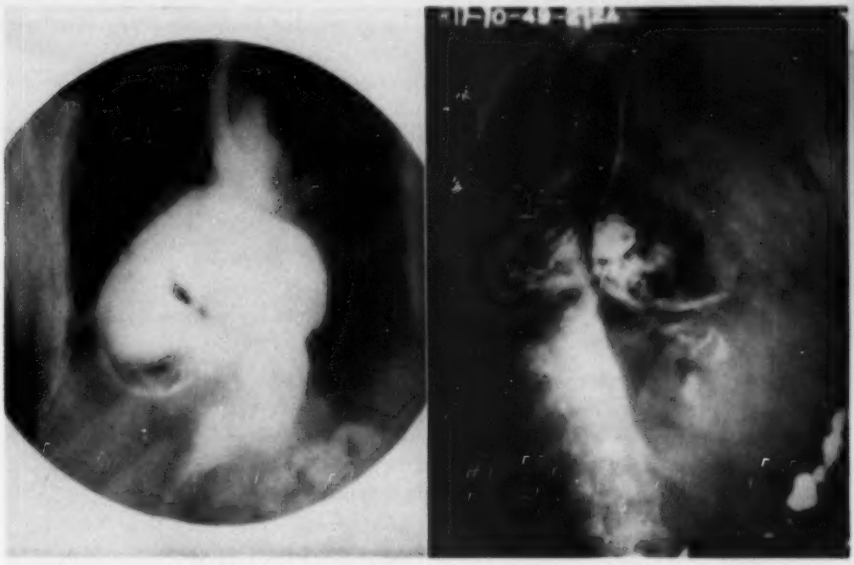


Fig. 1 Fig. 2

Fig. 1—Anteroposterior.
Fig. 2—Lateral film with tube in situ.

usually occurs much sooner after recumbency. It is present in fully 50 per cent of cases. It is characterized by its radiation into the neck, left shoulder and down the arm. It may very closely simulate that of angina pectoris, but is relieved by hypodermics of atropin or other antispasmodics, and is not in any way alleviated by nitroglycerin.

Pain may be induced immediately after a large meal, and pain in the epigastrium in an elderly, obese woman may be aggravated by lying down, and relieved by standing up. Small frequent meals will often relieve the distress. Straining at stool, coughing and sudden twisting of the body will aggravate it.

Emptying of the pouch above the stomach, either by emesis or the use of a gastric tube, relieves most of the symptoms.

It is characteristic of the pressure pain that it occurs higher than in the ordinary case, being present behind the sternum rather than in the epigastric area.

Dysphagia is not an unusual accompaniment and is due to constriction, particularly of a small opening, and interference with the circulation of the enclosed organ. This occurs in about 20 per cent of cases, resulting in severe congestion of the stomach. In at least 10 per cent of cases it proceeds to actual ulceration which is aggravated by the hurried swallowing of food, as well as taking rough or undigested food, very dry foods or hot liquids. This variety of dysphagia is relieved by antispasmodics, alkalis and aluminum gels.

The occurrence of ulceration explains the pronounced anemia which is often present. The anemia may be intermittent in type, due to intermittent bleeding. Hemorrhage may consist of frank hematemesis of large amounts, in which case the anemia is understood. In other cases, however, small, constant bleeding results in a very severe type of hypochromatic microcytic anemia. Most of the hemorrhages are due to actual ulceration of the mucosa proximal to the site of constriction. Some patients have hematemesis and melena, but no anemia, whereas others have anemia and no hematemesis. Blood in the stool is present in only about 33 per cent of cases.

In a group of these cases, studied at the University of Indiana, pronounced anemia was present in a large proportion of the chronic cases. This demonstrates that in unexplained anemia diaphragmatic hernia must be suspected as a casual factor.

In a few of the series of cases studied, however, was dysphagia a prominent factor of the disease. Heartburn, flatulence and regurgitation may be concomitant, but are in no way diagnostic. Vomiting is present in the advanced cases and usually relieves the distress, especially after a heavy meal. There is no distress after a light meal. Usually there is no disturbance of bowel function, unless the colon is involved in the process.

The thoracic symptoms occur less often than the abdominal symptoms and are dependent upon pressure on the heart or lungs. In the former case palpitation, tachycardia, and even auricular flutter has been reported. Dyspnea is a far more frequent symptom and may be a sequel of anemia or due to cardiac embarrassment. A dry, irritative cough does not come from the pharynx or bronchi, but is the result of nerve irritation. The constitutional symptoms are those of weakness and anemia.

Cases should be divided into two groups: those that are really symptom-free, where the diagnosis is made during the course of a routine gastrointestinal study, and those which present constant symptoms of the type already indicated. The latter group should be divided into the category of those presenting symptoms of a mild degree, occurring almost daily, and those characterized by severe attacks. In the latter, the constriction of the opening of the diaphragm becomes irritated due to overloading of the contained organ, usually the stomach, producing attacks of agonizing abdominal pain of a colicky nature, accompanied by vomiting. In the

case described in this study, these attacks were very characteristic, occurring after sleep, somewhat assuaged by assuming the erect posture, and practically relieved by emptying the contents of the stomach by lavage.

The clinician must be conscious of the possibility of hiatus hernia, but roentgenologic examination may be necessary for the final diagnosis. X-ray films taken in the Trendelenburg position are often of assistance, as also are methods that cause increased intraabdominal pressure by constricting bands.

To ascertain the length of the esophagus it is helpful to have the patient swallow a tube and pass barium through it under the fluoroscope. Determination of the exact location of the termination of the esophagus and its junction with the stomach is one of the most important diagnostic points. In addition, certain variations

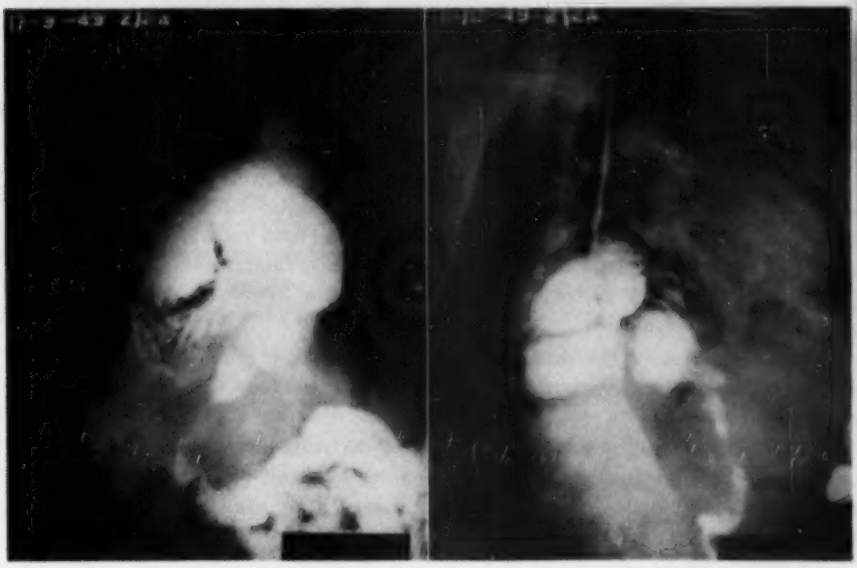


Fig. 3 Fig. 4

Fig. 3—Anteroposterior.
Fig. 4—Lateral film with tube in situ. Stomach partly filled.

of the esophageal function characterized by an extension of the column of barium holding four or five inches above the cardia is characteristic, and tortuosity of the esophagus, undoubtedly due to strangulation, is a further factor.

The lateral film is of value in determining the anteroposterior position of a diaphragmatic hernia.

Many cases of esophageal hiatus hernia are even recognizable in the erect position.

With the tube in the stomach, the characteristic lateral rugæ of the stomach are seen. When it is in the esophagus, the characteristic peristalsis of the esophagus can be noted, but no rugæ are present.

It is advisable to take the films immediately after the barium is ingested. If the hernia is large enough it is possible to demonstrate the mucosal folds. It also is advisable to examine the patient in the Trendelenburg position because in that position the hernia will be largest, and it is important from the standpoint of treatment because herniæ which contain over half the contents of the stomach are always surgical cases. Since much of the stomach is in the hernial sac it constantly increases in size until it approaches the point of strangulation.

It is necessary to make complete x-ray studies in the right and left and both lateral and oblique positions to determine the relationship of the herniated organ to the other viscera in the thorax.

When a hiatus or other diaphragmatic hernia is discovered, investigation should not be discontinued until a complete study of the gastrointestinal tract is carried out as this may disclose further lesions which are often more important. A case in point is one of pain in the upper left quadrant in which a hiatus hernia was discovered, but on further examination cancer of the descending colon was found to be the prime cause of the patient's symptoms.

In the few cases of complete inversion of the stomach with hiatus hernia, the cardiac portion of the stomach remains in the abdomen, while the remaining portion is inverted in the thoracic cavity. In such cases two air bubbles are usually seen in the flat x-ray plate, one in the superior normal fundus and the other in the pouch of the stomach above the diaphragm. Such a finding is practically diagnostic of hiatus hernia.

In eventration of the diaphragm or an abnormally relaxed diaphragm, the entire outline of the diaphragm can be seen in the rœntgen film, and there is no defect present.

The x-ray is also of value in determining the condition of the esophagus. In some cases a tumor involving the esophagus will shorten it without causing obstruction, but by shortening the esophagus it may draw the stomach through the hiatal opening, producing a hernia which is, in effect, due to a diseased condition of the esophagus.

There is apparently little difficulty in the differential diagnosis between a diverticulum of the esophagus, which has a perfectly round, smooth lumen, devoid of rugæ, in contrast to the rugæ which are seen in the lumen of the stomach in a hiatus hernia.

When the symptoms simulate the peptic ulcer syndrome the x-ray will provide the correct diagnosis.

The finding of a diaphragmatic hernia, especially a hiatus hernia, immediately demands a series of cholecystograms, and the diagnosis of a diseased gallbladder, if only suspected, demands surgery because the frequency of disease of the gallbladder causes irritation and shortening of the esophagus by reflex action of the vagus. Removal of the gallbladder repeatedly has eliminated esophageal hiatus hernia.

Anginal symptoms are frequently suggestive, but angina is apt to affect men more than women, whereas hiatus hernia occurs more often in women. Anginal pain is brought on by exertion while hiatus pain is relieved when the patient stands or sits up. Anginal pain is relieved by rest, whereas that of hiatus hernia occurs on lying down and is relieved by the erect posture. Nocturnal pain indicates hiatus and the pain of a hiatus hernia is relieved by belladonna or other antispasmodics, but not by nitroglycerin. In coronary conditions, on the contrary, nitroglycerin is most effective. It is a peculiar fact that amyl nitrate may relieve both conditions. Of course, the electrocardiographic findings should always be studied. We should not lose sight of the fact that the two conditions may coexist.

It is worthy of note that, at times, the pain projects beneath the left scapula.

Herniæ with large necks cause little constriction and but few symptoms.

Variable symptomless periods are due to spontaneous reduction of the hernia.

Carcinoma of the stomach should be excluded by rœntgenologic examination. It has been observed that hiatus hernia, despite the irritation caused by constriction of the enclosed gastric mucous membrane, is very seldom the site of malignant lesions, in fact, far less frequently than the average stomach, the hiatus hernia apparently offering some protection. Cancer of the stomach, however, below the hernia, is not rare. Esophagitis, peptic ulcer of the esophagus, and often cirrhosis of the esophagus may be present.

Esophagoscopy is an important adjunct in the diagnosis and no study can be considered complete until the esophagoscope has been used.

Perineoscopy as a means of diagnosis has some adherents.

Congenital herniæ in children belong to the surgical group; the majority are due to congenital malformations. The mortality in this group is rather high. Traumatic herniæ are now being treated successfully by the type of surgery indicated in the individual case.

The herniæ occurring in old people are those most frequently seen in the office of the gastroenterologist. These cases can be divided into three categories:

1. The mild asymptomatic type discovered in the course of a routine gastrointestinal examination. As a rule, these need no treatment other than reduction in weight and caution against undue straining and any effort which will increase intraabdominal pressure.

2. Patients with a small hernia and mild symptoms are best treated by reduction in weight, thereby diminishing the intraabdominal fat, by small meals at frequent intervals, and by the use of antispasmodic drugs, such as novatrin, atropine, trasentin, syntropan or papaverin. Many patients do well on a peptic ulcer regimen with the aluminum gels. They are instructed to avoid all exercise which increases intraabdominal pressure, and wearing tight-fitting corsets, and bands over the abdomen. Often eating in the standing position and refraining from lying down for an hour or two after meals will prevent the return of pain. In cases where a large portion of the stomach is above the diaphragm, the passage of a tube and

washing out the stomach at night enables the patient to sleep. Sleeping in a sitting position is of help in many cases. Small doses of nembutal at night are also helpful.

In the presence of gallbladder disease cholecystectomy should be considered.

3. The cases that fall into this group are definitely surgical.

Prior to any operation, be it abdominal or thoracic, the phrenic nerve should be crushed, and in cases of large congenital defects the nerve should be severed. Crushing of the phrenic nerve, usually on the left side, is a palliative; it relaxes the diaphragm and allows the organs to return to their proper place in the abdomen. The crushing operation should be used first as this causes a temporary paralysis of the diaphragm lasting 6 to 8 months. If avulsion of the nerve is done, it causes permanent paralysis of the diaphragm with resultant wasting of the diaphragm, and if surgery becomes necessary later, there is less tissue available for repair.

In the past decade there has been an increasing resort to surgery in hiatus hernia, the indications being intractable pain with frequent episodes of vomiting, pronounced anemia, and over one-half of the stomach above the diaphragm. The pioneer work of Truesdale has been supplemented by the much larger experience of Harrington, of the Mayo Clinic, who has now operated upon nearly 400 cases. He prefers the abdominal approach because any other abdominal lesions which may be present can be cared for at the time of operation. All left-sided herniæ can be handled through this approach. The operation is done by approximating the surface with silk mattress sutures, reinforced by live fascial strips interlaced over the proximal margins. In the hiatus variety it is essential that an Ewald tube be *in situ* so that no constriction of the esophagus will result. Removal of the sac is an essential part of the operation. The sac probably is a union of the peritoneum and the serous surface of the stomach, and some difficulty may be experienced in its removal.

The European approach to the operation is mainly through the thorax, but it would appear from a study of the operative mortality and the end-results that the abdominal approach is the preferable procedure, certainly in the hands of American surgeons.

In true right-sided herniæ, where the large size of the liver renders inaccessible the site of operation, the operation should be done through the transthoracic approach. The case should be completely studied to determine the exact site of the herniation, as the mass of the stomach may be projected to the right over the liver with the actual hernial opening in the region of the hiatus and proper for abdominal approach.

BIBLIOGRAPHY

Benedict, E. B. and Sweet, H. H.: Benign Stricture of Esophagus: Special Reference to Esophagitis, Hiatus Hernia, Esophageal Ulcer and Duodenal Ulcer. Year Book of Medicine. The Year Book Publishers, Chicago, 1949, 649-650.

Bockus, H. L.: Diaphragmatic Hernia Including Esophageal Hiatus Hernia and Eventration of the Diaphragm. Gastroenterology, Vol. I. W. B. Saunders, Philadelphia and London, 1944, 151-168.

Branwood, A. W.: Esophageal Hiatus Hernia. Edinburgh M. J. **55**:50-58, (Jan.), 1948.

Brown, C. F. G. and Dolkart, R. E.: Significance of Gastrointestinal Tract Abnormalities as Related to Management of Cardiac Disorders. Year Book of General Medicine. The Year Book Publishers, Chicago, 1944, 565-566.

Candolin, Yngve: On Diaphragmatic Hernia. Acta Chir. Scandinav. **95**:61-75, 1947.
Chevallier, Paul and Danel: Chlorotic Anemia and Diaphragmatic Hernia in an Aged Woman. Year Book of General Medicine. The Year Book Publishers. Chicago, 1946, 469-470.
Gilbert, N. C.: Recurrent Esophageal Hiatus Hernia. M. Clin. North America. **32**:213-222, (Jan.), 1948.
Glass, Jerzy: Przepuklina Przeponowa Soladka. Polska Gazeta Lekarska. **41**, 1945.
Guthrie, D. and Jones, F. H.: Diaphragmatic Hernia. The Year Book Publishers, Chicago, 1941, 533-541.
Harrington, S. W.: Various Types of Diaphagmatic Hernia Treated Surgically: Report of 430 Cases. Year Book of Surgery, Chicago, 1948, 617-619.
Hodgson, J. R. and Kirklin, B. R.: Roentgenologic Characteristics of Diaphragmatic Hernia. Am. J. Roentgenol. **58**:77-102, (July), 1947.
Hughes, F., Kay, E. B., Meade, R. H., Jr., Hudson, T. R. and Johnson, J.: Traumatic Diaphragmatic Hernia. Year Book of General Surgery. The Year Book Publishers, Chicago, 1948, 615-617.
Marks, Joseph H.: Esophageal Hiatus Hernia with Inversion of the Stomach. Am. J. Roentgenol. **60**: 63-68.
McNealy, R. W. and McCallister, J. R.: Transabdominal Repair of Esophageal Hiatus Hernia. Year Book of General Surgery. The Year Book Publishers, Chicago, 1947, 541-547.
Pavlovsky, A. J.: Diaphragmatic Hernia. Year Book of General Surgery. The Year Book Publishers, Chicago, 1943, 510-518.
Phillips, J. R.: Diaphragmatic Hernia. Year Book of General Surgery. The Year Book Publishers, Chicago, 1944, 535-536.
Radoff, F. F. and King, R. L.: Esophageal Hiatus Hernia. Gastroenterology. **9**:249-252, (Sept.), 1947.
Ritchey, J. A. and Winsauer, H. J.: Anemia and Its Relation to Diaphragmatic Hernia. Am. J. M. Sci. **214**:476-482, (Nov.), 1947.
Rosenberg, H. N. and Rosenberg, I. N.: Simultaneous Association of Situs Inversus, Coronary Heart Disease and Hiatus Hernia. Report of a Case and Review of Literature. Ann. Int. Med. **30**:851-859, (Apr.), 1949.
Trueman, K. R.: Diagnosis and Treatment of Paraesophageal Hiatus Hernia. Canad. M. A. J. **56**:149-153, (Feb.), 1947.
Truesdale, P. E.: Diaphragmatic Hernia. Year Book of General Surgery. The Year Book Publishers, Chicago, 1945, 525-531.

TREATMENT OF GIARDIASIS BY THE CHLOROGUANIDE CHLORHYDRATE

ALBERTO ALBORNOZ PLATA, M.D.
Bogotá, Colombia

Introduction

This experimental work deals with the use of an antimalarial drug, the chloroguanide chlorhydrate, in people infested with giardiasis; this work was started, observing that other antimalarial drugs, such as atabrine and cloroquine have a certain action on this intestinal parasite.

The patients who were treated with this medication attended the prenatal and pediatric clinics of the Model Health Center, a subsidiary of the Cooperative Interamerican Health Service which checks about 55,000 people in the Zone VI of Bogotá. Almost all of these belong to the lower and labor classes. The sanitary conditions of this zone (water supply and sewage) are perfectly good, but the food supply and its preparation in general has many deficiencies.

Giardiasis

The giardiasis is a universal parasitosis; many times not causing any symptoms and at other times its eradication does not give the patient the relief of the symptoms which were thought to be caused by the giardia. It is a flagellate protozoa and reaches the organism through food and water, contaminated with feces, containing the cysts which establish in this way the transmission of the disease. Under the epidemiologic point of view it is important to recall that the dog frequently harbors the parasite in its intestines. In the human being it lives in the duodenum and may pass into the biliary tract. The parasite is easily found in the duodenal drainage and for this reason some authors believe that it has a great importance in the biliary tract diseases (very little according to Bockus).

The giardia reproduces greatly in the colon and produces colonic trouble resembling dysentery of short duration. In these cases the trophozoite can be observed through the coprologic examination, but almost always, one finds the cyst with this laboratory test and the diagnosis is made in this way.

Some times, later controlled by treatment, the giardiasis may produce a lot of nervous digestive troubles, as shown later by the success of treatment (W. C. Alvarez).

Chloroguanide

This drug which gives excellent results in the treatment and prophylaxis of malaria, was one of the products of World War II.

It is an antimalarial drug, chemically completely different from the quinine and chloroquine, which are quinolein derivatives, and from the atabrine that is an acridine. The chloroguanide is obtained from the anilopyridine and has the biguanide radical in its composition.

It is a base and can be combined to give salts, like chlorhydrate which is the one most commonly used; it is hydrosoluble, white and of bitter taste; the solution can be boiled and the drug is not destroyed.

Using it orally its absorption is very complete and after two hours the blood concentration is quite satisfactory.

The drug is mainly eliminated through the urine and feces and probably this latter way of elimination should explain its action on the giardias.

It is a nontoxic drug, and its therapeutic doses (0.25 gm.) is very far from a toxic dose.

It also goes under the trade name of Poludrine (England) and is frequently designated under the key number 4.888; it is marketed in 0.29 gm. tablets and is prepared by Squibb laboratories.

Giardiasis in a Zone of Bogota

I believe that it is of some interest to observe the following data dealing with the monthly coefficients of giardiasis in the year 1948.

TABLE I

Month	Total Feces Ex.	Total positive for giardiasis	Coef. %
January	269	64	24
February	225	41	18.2
March	210	42	20
April	107	19	17.8
May	153	36	23.5
June	118	10	8.5
July	90	9	10
August	108	9	8.3
September	169	21	8
October	134	21	15.6
November	106	7	6.6
December	87	8	9.2

It is remarkable to observe the progressive fall of the coefficients since July, except for October, when for unknown causes there is a recurrence of the parasitosis. I think that the general health education has played a great role in this program. In the last year, 1948, we did not give any treatment for giardiasis, so that this cannot be the cause in the fall of the coefficients.

Chloroguanide and Giardiasis

We used the drug in patients of both sexes, in adults, children and prenatal patients. We studied 20 cases, 12 adults and 8 children and the result of the treatment was checked by fecal examinations done the day after finishing the treatment. The age limits were 1 and 32 years.

The coprologic examinations (before and after treatment) were made by the concentration technic (U.S. Army method).

The treatment was carried out in the following way: The adults received a tablet daily during 8 days; the children received the drug according to age, more or less 0.02 gm. per year, until 6 years of age.

All the cases gave negative coprologic results after this treatment. There was never observed any case of drug intolerance nor other reactions; the prenatal patients tolerated the drug well and pregnancy was not interrupted by this therapy. During the 8 days of treatment with chloroguanide no other drugs were used. The children also showed good tolerance.

The following table shows the results obtained:

TABLE II

Results of the Chloroguanide Used in the Treatment of Giardiasis

Case	Patient	History	Age	Coprol. ex. Giardia	Chloroguanide		Coprol. ex. giardia after treatment	Observations
					Dose per day	Number of days		
1	M.M.	260–3	1	x	0.02	8	(-)	
2	C.M.	1493–3	25	x	0.25	8	(-)	Prenatal
3	S.S.	4376–4	30	x	0.25	8	(-)	Prenatal
4	H.R.	1447–3	22	x	0.25	8	(-)	Prenatal
5	P.R.	6327–2	22	x	0.25	8	(-)	Prenatal
6	S.Y.	4885–3	5	x	0.10	8	(-)	
7	G.Z.	2292–3	26	x	0.25	8	(-)	Prenatal
8	J.G.	635–3	2	x	0.04	8	(-)	
9	N.G.	1797–4	3	x	0.06	8	(-)	
10	G.M.	2020–4	21	x	0.25	8	(-)	Prenatal
11	V.S.	2822–4	3	x	0.06	8	(-)	
12	G.M.	925–3	32	x	0.25	8	(-)	Prenatal
13	S.A.	6706–2	23	x	0.25	8	(-)	Prenatal
14	C.E.	1987–1	26	x	0.25	8	(-)	Prenatal
15	M.M.	3831–3	28	x	0.25	8	(-)	Prenatal
16	J.G.	764–5	4	x	0.08	8	(-)	
17	F.R.	5531–5	19	x	0.25	8	(-)	Prenatal
18	L.M.	2443–3	27	x	0.25	8	(-)	Prenatal
19	B.A.	3883–5	2	x	0.04	8	(-)	
20	D.L.	2265–1	3	x	0.06	8	(-)	

Results

The results obtained were excellent, inasmuch as the chloroguanide was effective in 100 per cent of the cases. It should be expedient to handle a larger group. The dose used is similar to the one used in malaria, but it is possible that smaller doses may be effective. Also it could be studied when the fecal examinations become negative, since in the course of treatment it is possible that this may occur before the 8 days.

Conclusions

1) — The chloroguanide is effective in the treatment of giardiasis.

2) — The daily dose of 0.25 gm. during 8 days in adults and the 0.02 gm. per year of age in children is effective.

3) — Intolerance or side-effects to the drug were not observed with the above doses.

4) — The children tolerate the drug well.

5) — The pregnant women did not show changes, and therefore this state is not a contraindication to the drug.

SUMMARY

In treating 20 cases of giardiasis, 12 adults and 8 children with an antimalarial drug, chloroguanide, the effectivity of the therapy was checked by fecal examinations. The results obtained were excellent, since the drug was effective in 100 per cent of the cases.

This work must be followed-up by investigation in larger groups and also looking for a shorter duration of this therapy.

The author is very much indebted to the E. R. Squibb and Sons Laboratories for having supplied the drug necessary in this work.

BIBLIOGRAPHY

E. R. Squibb and Sons: "Los paludismos y su tratamiento." (pamphlet)
Falla, Luis A.: "Estudio comparativo entre el 4888 y el SN 7618 en el tratamiento del paludismo". Rev. Med. y Cir., (March 1949).
Bockus: Gastroenterology Vol. III, (1946), Saunders & Co., Philadelphia, Pa.
Alvarez, W. C.: Nervousness, indigestion and pain. Paul B. Hoeber, N. Y.
Beckman: "Treatment in general practice". Saunders & Co., Philadelphia, Pa. (1949).

CORTICODIENCEPHALIC GASTROINTESTINAL SYNDROMES IN EPILEPTICS*

Part VII

THOMAS S. P. FITCH, M.D., F.A.C.S.†
Plainfield, N. J.

ALBERT W. PIGOTT, M.D., B.S.**
Skillman, N. J.

and

SAMUEL M. WEINGROW, M.D.††
New York, N. Y.

Neurophysiology

Under this heading two approaches to the corticodiencephalic system are to be considered, namely, the neurophysiology of the gastrointestinal tract as far as its corticodiencephalic control and the neurophysiology of the convulsive mechanism. Although it has not been our habit to take stands or present issues unbacked by the literature, we will break our routine at this point. We wish to go on record that we feel that anatomically, physiologically and clinically, there is a parallel line of activity between the convulsive reaction and manifestations of gastrointestinal interruption of function in the same way as the former runs parallel with pupillary changes in almost every epileptic fit. That both of these problems are intimately related has been shown by the fact that even during an ordinary convulsion, gastrointestinal phenomena such as salivation, defecation and occasional vomiting occur. Other autonomic manifestations of the gastrointestinal activity during an ordinary convulsion have previously been mentioned.

First we shall confine ourselves for only a short time to the neurophysiology in respect to the neurogenic control by the corticodiencephalic system and by the corticopyramidal and spinothalamic tracts thereby exerting a definite effect upon the gastrointestinal activity not only in the epileptic but also in other neurological conditions. Since we have so repeatedly referred to the work of a great many experimenters on the relationship between the mammillary and adjacent structures controlling gastrointestinal tract and water metabolism; and, moreover since we have dwelt at a great length on the cortical control of the gastrointestinal and urinary function as elaborated by Watts and Fulton and Watts and Frazier, it will be highly superfluous for us to waste the time of the reader by incessant repetitions. Figs. 2, 3, 3a, 4, 5, 7, 8, 9, 10, 25, 26 offer a sufficient review.

Here, we must however definitely state our position that we have no axes to grind over our view either in relation to the corticothalamomammillary tract or to the pyramidal and spinothalamic tract in so far as their neurogenic control of

*Read in part before the Thirteenth Annual Convention of the National Gastroenterological Association, New York, N. Y., 7, 8, 9, 10 June 1948.

†Chief Neurosurgeon, New Jersey State Village for Epileptics.
**Medical Superintendent, New Jersey State Village for Epileptics.
††Assistant Neurosurgeon and Research Neurologist, New Jersey State Village for Epileptics.

gastrointestinal and urinary functions are concerned. Whether it will be shown eventually that the former contains both sympathetic and parasympathetic fibres, or that it contains one type of fibre system, and that the spinothalamic system extending into the cortex is responsible for the centripetal and that the pyramidal tract is responsible for the centrifugal fibres to the gastrointestinal urinary tract or other portions of the autonomic nervous system, will eventually be decided by specialists, who, in their pharmacologic pursuit, will make that decision one way or another. At this point we should not neglect the extrapyramidal views of Watts and Fulton. We know that there might be a connection between the striatal system and the spinothalamic system. The medial lemniscus, for instance, is known to supply collaterals to the substantia nigra and the hypothalamus which is also connected in some places to the lenticular nucleus. It also contains a subthalamonigral pathway. Whether this relation is for tonus and motion or for gastrointestinal control, remains to be seen. For this reason we have offered a very extensive anatomy of the mammillothalamic tract and the final common pathway with experimental results, so that an investigator may pursue experiments along one line or another. The neurophysiologist of the future will have to explain the multilocalization of head, eye and pupillary movements as well as the multilocalization of the sympathetic and parasympathetic in the cerebral cortex. The electroencephalographer will demand a thorough autonomic cerebral neuroanatomy for his use in the same way as the electrocardiographer must have the anatomy of the bundle of His and its distribution in all heart chamber walls. Our extreme efforts with the extensive neuroanatomy which we presented in the previous pages had, as one of its prime objects, the mapping of cortical function so that its electrophysiology could be established. Eventually we will have to know why we have crests and troughs in brain waves, and which is due to motor, which to sensory, which to autonomic, which to A B C conduction and which to projection and association pathways? For head movement reference see Fig. 30.

We repeatedly referred to the work of Muskens who showed, that during a convulsion which had been induced either by a sympathetically acting drug or a parasympathetically acting one, there is hardly any difference between the type of convulsion whether tonic or clonic or its other accompaniments. For these and other trigger zones see Fig. 33.

In favor of the mammillothalamic and mammillosupraoptic schools whether it contains the sympathetic fibres or parasympathetic fibres or both it may be said that it does not appeal to the reason of the neurophysiologist that such a tract stands alone and has done so for a very long time without anyone attaching some functions to it. Although fibres extend from the anterior nucleus of the thalamus into the cerebral cortex in such a locality, there are a great many extensive functions referring to the gastrointestinal tract, not only to its smooth musculature but also to the adjuvant functions such as rhythmic chewing, swallowing, localization, salivation, motion and tone. Yet, no one has ever coordinated all the above functions and attached them to this most interesting reticulocortical pathway. It stands to reason that this pathway, by virtue of it being more of a fasciculo-

nuclear tract, probably bears extensive chemotropic functions as well as having a specialized form of C-conduction fibre system which is characteristic of the autonomic. This tract should be of extensive interest to the bioelectric neurophysicist because it probably contains extensive C-fibre systems within are slow conduction transmission pathways. The extensive internuncial apparatus within the diencephalon and the tremendous hookups which such an internuncial system affords in relation to the mammillothalamic tract makes it reasonable for one to assume that such a system would carry the tendency toward the permanency of rhythmic bioelectric impulses which are the result of gastrointestinal, urinary, respiratory, cardiovascular and other impulses, probably due to action currents of a permanent nature that exist in the life of the individual whether asleep, awake or even in coma. Here we must caution the reader regarding our reference to the mammillothalamic. We previously expressed our wish to include the dorsal longitudinal fasciculus, the preoptic components of the striae terminalis, Ganser's and Meynert's commissure and the pedunculotegmental system under this term. In this way we felt that the experimental results of the Beattie, Sheehan, Keller and D'Amour gastrointestinal school and the work of the great number of experimentalists on water metabolism will find a neuroanatomic substratum. Whether such a system exists, with its continuous action currents which are either generated by contraction of smooth musculature or by cell groups centripetally from certain centers within the diencephalon, remains to be determined. It is not impossible for such a system to send out fibres to various lobes of the cerebral cortex, as we have shown and thereby be a factor in the production of parts of the potential which we see in the electroencephalogram in the normal physiology of the human individual. Whether the dominant rhythm during sleep, which occurs in every portion of the cerebrum, contains an autonomic bioelectric factor remains to be determined since autonomic activity might in part be responsible for the slow sleep potentials.

The work of Kornmuller on the various types of potential wave patterns might point to the diencephalon as a center for the origin of potential of various magnitudes which is distributed throughout the various cortical areas upon reaching which the wave pattern, as seen in the electroencephalograph, becomes changed and modified or, because essentially consisting of various A, B and C frequencies, the cortex has a potential which is different from that seen in lower structures of the diencephalon. Not only is the work of Kornmuller important in epilepsy but the paper by Ward (1948) shows that all is not well with our modern relation of brain waves to the cortical pattern. Our concentration upon anatomy and particularly on the work of cortical function by Davison and Goodhart as well as upon Penfield was for the purpose of stressing the blueprint of the cerebral cortex. The synchrony of bilateral leads might be explained by a diencephalic or a corpus callosum mechanism, but before that is done we must know why we have crests and troughs in brain waves. The only time we shall be able to offer a logical explanation of this will be when we have mastered the anatomy of the cerebrum. Maybe the substratum of these activities is in the possible implication by Rosett

that the vertebrate kingdom consists of a neurotopographic bicellular structure both anatomically and physiologically through the pyramidal system. Not only for the above reason is the mammillothalamic important but also because some years ago one of us (Weingrow), attempted to point out (1932) that in each epileptic attack there is a concomitant contraction of the smooth musculature of the entire intestinal tract. At that time the equipment in the laboratory in which he was working was not available to show cinematographically that contractions of the gastrointestinal tract occur with every epileptic attack. This did not include Jacksonian seizures, otherwise localization would be in the corticospinal region. But not before the publication of his paper (1932) did another worker produce definite evidence, by means of movie films, that such contractions do occur. It seems that very few references, if any, to this phenomenon have since then been made. It is up to experimentalists to continue such work. If definitely substantiated, it would show that every individual, whether suffering from epilepsy, or the convulsions of brain tumor, has associated with it the convulsive manifestations of gastrointestinal disturbances. It stands to reason that if the gastrointestinal smooth musculatures contract during a fit that the genitourinary musculature should follow suit. Whatever the significance of the smooth muscle convulsion may be, if we concentrate on this phenomenon too much and overstress it we will bring upon us the unwelcome criticism that might be brought against Muskens. After all his outstanding work on the myoclonic reflex he about-faced with the statement that there is no "Krampfenzentrum" and that there isn't even an anatomical location for the grand mal convulsion. We don't wish to add to this argument a center for the bilateral smooth muscle contraction. If there is such, the modern bioelectricians, who are attacking the problem anatomically by differentiating the afferent from the efferent brain wave manifestations of the fit, should do the tracking down. We heartily agree with their following Jackson instead of Muskens as we have shown. If the smooth musculature neurogenic tract within the brain controlled the entire smooth musculature apparatus it is not unreasonable to assume that the cardiovascular musculature system also contracts during a non-Jacksonian epileptic fit. If this occurs, as is definitely substantiated by the change in the heart rhythm and in the pulse during a fit, then the internist has a tremendous problem in the diagnostic as well as therapeutic procedures which should ensue in the handling of autonomic phenomena accompanying the convulsion, because these would involve every organ and system within the body aside from the usual musculoskeletal system and implicate sympathetic and parasympathetic pharmacology.

At this point we can send our imagination into a whirl by elaborating further upon the effects not only upon the gastrointestinal system, water metabolism, but other systems that contractions of smooth musculature would involve in the course of a convulsion. We can for instance, side with Temple Fay and his hydrodynamic theory of the production of seizures. We can furthermore say the edema of the brain, incidental to convulsions, might be due to a slowing up of the usual vascular contractions because the fit has produced a change in rhythm of

the smooth musculature by interference in conduction of synchronous impulses. Whether one came first, and the other second, or vice-versa, is unimportant in so far as the function of the autonomic is concerned. This, however, points to the fact that Temple Fay might have been correct and that water collections within the brain in relation to convulsions are really concomitants of a seizure whether they are upsetting the water metabolism or not. In all our work up to now, and in subsequent efforts in this paper we have been cautious not to inject our own opinions or stress any pet theories. We have emphasized the myoclonic shock view because it has a physiologic approach. It does not cover migrating sensory phenomena which Muskens himself stressed in sensory fits and in the reflex and sensory findings on neurological examination. We have concurred with him and made these reflex and sensory observations for over two decades. For this reason we disagree with a purely motor theory. We therefore wish to go on record as favoring a view of migrating potential. At present we cannot elaborate upon our concepts but we have enough clinical subjective and objective material to make the generalization that epilepsy is merely a disturbance in the pulsating central excitatory state producing sensory reflex, and motor after-effects.

The above problem and other numerous ones can be brought in for the purpose of elaborating upon the findings during one experiment. We would however call down upon us extensive criticism were we to invoke more references from the literature to show that, chemically or experimentally, such a phenomenon exists. Our interests are however not in that direction at all. They are largely in the direction of the corticomammillothalamic tract which stands alone as a neglected neuroanatomic orphan in the entire field of neurophysiology and neurology. It is high time that this structure be given the consideration due to it. The reason for such neglect however, has been the indecision by anatomists to establish this system in conjunction with the corticosupraopticomammillary tract as a definite entity. There is no reason why the neurophysiologist could not use it. The extent and dimension of the fibre system suggests that this tract probably contains centrifugal as well as centripetal fibre systems not only to the gastrointestinal and urinary tract but also probably to the cardiovascular and genital systems. Kappers, Huber and Crosby would probably disagree on the afferent point. Their view is that the diencephalic region, particularly the optic thalamus like the mesencephalon, should be divided into a dorsal sensory and a ventral motor sector. It is probably in this tract and in the related structures that not only gastrointestinal, urinary, metabolic, cardiovascular, but other functions, especially those of a trophic nature, are carried. In our institution we have one or two cases of hemihypertrophy of the body, yet in these patients there are few evidences of extensive gross encephalic involvement. The mammillary bodies seem to carry the phylogenetic body size function. A small lesion in one side might be conceived as being responsible for a hemihypertrophy. In such a tract as the mammillothalamic, and in that only, it seems that a lesion could produce a phenomenon as hemihypertrophy with very few neurological positive findings. We have encephalographed one of these patients and will some day publish the exact results of the air studies.

We were rather brief in the dealing with the corticothalamomammillary tract in relation to its neurophysiology concerned with gastrointestinal and urinary function. Had we been somewhat more pedantic, we might have applied the term of somatotopic localization of the gastrointestinal and urinary function within the diencephalon in the same way as Wartenberg did with the localization of trophic function. Evidently we did not care to have some one bring down upon us the neurologic gavel in the same way as Archambault and Fromm did upon Wartenberg. In some pages in our discussion of spasmodic conjugate deviation of the eyes and head as presented by Davison and Goodhart, we showed that the term somatotopic was applied to the optic thalamus. Davison and Goodhart are experienced neuropathologically and clinically as seen from their publication records. With the term somatotopic they probably had in mind not only the immediate vicinity of the extrapyramidal but the substantia nigra and even the cerebellum and inferior olivary body. These structures, particularly the last one, have oculogyric and neck movement functions. Aside from these specific cervical functions the body and extremities are well represented in them. In other works upon the basal ganglia Goodhart and others have attempted a somatotopic localization of various functions of an autonomic as well as extrapyramidal character within various structures of the cerebrum and diencephalon in particular. If this could be definitely proven within the human or in the diencephalic portion of the mammillothalamic tract we would not hesitate to so state. This is particularly applicable only to the lower portions of the corticothalamomammillary tract. The portions under consideration are restricted however to the thalamic and mammillary portion of the mammillothalamic tract. In the cortex however, there has been so much clinical and so much experimental evidence of definite localization of a somatotopic type referring to the gastrointestinal and urinary tract within various areas of the frontal lobe that an attempt to use this term cortical somatotopic localization of gastrointestinal and urinary function could be definitely termed as relevant. The reader should however understand that when we stress the cortical beginning or ending of the corticothalamommillary tract, we mean exactly this tract and no connections with the fibres of the pyramidal system. It must be remembered that Watts and Fulton as well as Spiegel and his associates referred to somatotopic localization in that the center for the bladder and the stomach were at the same level as metameric muscles of the musculoskeletal system in the localization level in the precentral pyramidal cortex. Stimulation of the areas of the cerebral cortex to produce stomach contractions and carrying out a similar procedure to produce unilateral convulsions are simple enough. The establishment of pathways for gastrointestinal movements and for generalized convulsions are however beset with tremendous difficulties. The reader has seen from the anatomical data which we presented what the problems under consideration are. It is easy to understand that progress made along the lines of solving the convulsion problem will also aid our knowledge of neurogenic gastrointestinal center oper-

ation. It seems from the pioneer work with the electroencephalogram that the former problem is being solved along anatomical lines of effects upon afferent and efferent stimulation, etc. Use Fig. 5 for neuroanatomy of Figs. 27 and 33.

Before going to the pyramidal school it seems to us that the essential difference between the mammillothalamocortical tract and the pyramidal system is that the former contains more neuron chains than the latter. In other words if a degenerative process starts in the former and such a process eliminates one neurone at a time, it is not as complete as in the latter because more neurons are situated longitudinally along the tract which is essentially a nucleofascicular tract. This is a commonly accepted principle. It is backed up by endless clinical experience. In other words the corticothalamomammillomesencephalic tract is more or less a compensation tract. Somewhere in the foregoing data and particularly in the literature (Pigott, Weingrow and Fitch 1939-1940) we brought up the problem of a chronic progressive degenerative bioelectric phenomenon. We pointed out that in certain diseases, once a process starts to progress, there is no turning back. A neural susceptibility gradient having a relation to some chemical catabolic process might be related to this. We pointed out that this condition is present in neurosomatic deterioration in epilepsy. It is also present in mesencephalic encephalitis which is characterized by progression in the form of Parkinsonism and its associated mesencephalic progressive vegetative disturbances. We finally also pointed out that it is present in brain stem and spinal disease such as amyotrophic lateral sclerosis. It might be advisable to designate this phenomenon in relation to the anatomical location as above successively the X, Y, Z, bioelectric progressive neurodegeneration. Not only the rapid form of the neurosomatic deterioration syndrome but the alarming sudden downgrade progress in amyotrophic lateral sclerosis, pseudobulbar palsy, and terminal brain conditions associated with hyperpyrexia as well as special types of diencephalic syndromes such as Simmond's disease and myasthenia gravis fall into this syndrome of chronic progressive descending vegetative diencephalopontobulbar degeneration. There is no doubt that some vital structures essentially located in the diencephalon might be the locus responsible for this phenomenon. The experimental work in the regions of the mammillothalamic and mammillosupraoptic systems point to this region as one of the most likely one to control the neurovisceral and neurosomatic destiny of the individual. The clinician encounters this condition in various etiologically different neurological disorders. Once this process starts it may have an acute or chronic cause, but there is no turning back. No therapeutic procedure thus far has been shown to be of help. It may be that our anatomical and physiological effort in the foregoing will shed some light on this phenomenon which has an autonomic and somatic feature. The autonomic of this phenomenon seems to be within the provinces of tonus and trophism and its location is in the Cajal-Friedemann loop.

In regard to the pyramidal and spinothalamic school in relation to their neurogenic control of gastrointestinal urinary and trophic function, it is needless for us to emphasize that we have covered a great deal of the physiology of this subject in the course of discussing the neuroanatomy. The trends of Watts and

Fulton, Watts and Frazier and isolated papers by Watts alone, some with definite clinical cases, indicate that somatotopic localization of the neurogenic control of the gastrointestinal and urinary tract within this system is more applicable and has a tremendous clinical background which is far superior than that found in connection with the corticothalamomammillary and corticosupraopticomammillary systems. It should be stressed here that what has been stated above with regard to the autonomic of the gastrointestinal applies to the autonomic of the convulsion because of it being essentially a phenomenon involving temporary change in muscle position including, reflex and tonus as well as muscle strength factors. It should therefore be related to the pyramidal pathways as well as to those of the corticodiencephalic autonomic. To confirm the above see Figs. 4, 27, 30 and 33.

This pyramidal avenue or the final common pathway system, consisting both of spinothalamic, pyramidal and possibly extrapyramidal, is a system which has been extensively worked up both clinically and experimentally. The neurogenic control of the gastrointestinal and urinary function by fibre paths which pass along the above extensive systems as part of the pyramidal avenue would derive a tremendous amount of benefit of exact localization on the basis of the association of gastrointestinal and urinary phenomena with other modalities such as sensation, motion, abnormal involuntary movements, visual perception, auditory, etc. It is along this pathway that centrifugal and centripetal directions of transmission of bioelectric representations of sensation and motion is definitely mapped out. In other words this system has been much more elaborately worked up than the corticothalamomammillomesencephalic and corticosupraopticomammillomesencephalic systems. We have seen above in the data from Davison and Goodhart that not only pupillary but particularly eye, head, neck and body movement throughout the cerebral cortex are associated with the final common pathway. This spinothalamic and pyramidal system, in addition to having definite connections via the spinothalamic cortical radiations with the optic thalamus and other definite evidence of parasympathetic centrifugal and centripetal fibres such as those that connect from the cerebral cortex to the trigeminal to the Edinger-Westphal nucleus, to the vegetative representative and the facial and the vagus nerve, is also one to which the terms sympathin and parasympathin may be applied more readily than to the corticothalamomammillomesencephalic system. At every opportunity we stressed the association and projection system described by Rosett in relation to the pyramidal pathway. We have even given him the credit of implying that, topographically along its longitudinal axis, the vertebrate kingdom is ontogenetically and phylogenetically a bicellular mechanism. That was done because the pyramidal pathway, which is so potent a structure, consists longitudinally of only two cells. If Rosett's simplification of the entire nervous system as consisting of merely motor and sensory components is true, then our problem of explaining the fundamentals behind the brain wave crest and trough becomes simple. The chances are that more than that will be required. The physics involved in A, B, C conduction and the roles of sympathin and parasympathin, etc. will have to be adduced in addition to the central excitatory state. Although we have the urge and

have from time to time in the foregoing had the tendency towards going off at an angle in our discussion of the term sympathetic and parasympathetic and elaborating upon the same, we consciously steered away from this subject because it would require too much space to do it justice. Now and then we referred to pilocarpine, and pituitrin as the parasympathin and in contradistinction to adrenalin and ephedrine which are sympathetic substances. The convulsive process like the gastrointestinal motor and secretory processes may therefore, by being a pyramidal system phenomenon, not be considered as shut out of physicochemical reactions that depend upon the action of sympathin and parasympathin. The relation of the motoneurons to acetylcholine and the chemical changes at neuromuscular junctions points towards an intimate relation between convulsive motion and the biochemistry of the autonomic.

We purposely steered away from the sympathin and parasympathin terminology although it has tremendous bioelectric physiologic significance on the basis of the role played by acetylcholine in nerve function. Sympathin and parasympathin may be related as has been shown by Rosett's references to Myerson and to many other drugs than adrenalin. Along bioelectric neurochemical lines, sympathin and parasympathin may be related to acetylcholine and eventually to phosphagen. The last mentioned substance is of course intimately connected with muscle metabolism. We refer the reader to this problem of sympathin and parasympathin which he may be able to find in the data as shown in the title of our bibliography. One more important aspect of this sympathin and parasympathin in relation to the corticodiencephalic neurogenic control of viscera by the autonomic system is that these and related substances have been called the neurocrines. They are related to the estrogens in the same way as adrenalin or sympathin are related in some physiological way to the cortical adrenal hormones. It is evident from the above that, just as adrenalin is related to chloride and water metabolism, so might some of the other substances in this group be related. The significance of the last two mentioned items is seen in their connection to our previous elaboration on water metabolism. The reader can therefore see how our delving into an extensive anatomical elaboration of the corticothalamomammillomesencephalic and corticosupraopticomammillomesencephalic tract in distinction to the final common pathway will help future experimentation in pharmacologic and neurobioelectric investigations.

Our chief interest in sympathin and parasympathin in their relation to the functions of the nerve tract mentioned above is the fact that the action of most of these drugs might be directly or indirectly connected with not only the neurogenic control of gastrointestinal function but also with the mechanism of the convulsion itself. We have repeatedly emphasized that a convulsion may be accompanied by mydriasis as well as myosis. This would indicate that, whether the sympathetic or parasympathetic system is aroused and accompanies the fit, it will have the autonomic motor and other manifestations with it. We referred to the autonomic data by Muskens who mentioned the work of Furstner on creatinin and the work of Pollack on pictrotoxin, who also produced myosis with both of the above drugs,

in contradistinction to mydriasis, which characterizes absinthe convulsions. Although we have stressed the work of Rosett, Greving, Malone and Muskens in this report and have concentrated on the diencephalon, stressing at the same time the importance of the pyramidal system, we haven't lost sight of a very important fact. It is the subject of the central excitatory state (C. E. S.) which seems to be the fountain, not only of tonus, but a factor in every convulsion. At one time we seemed optimistic enough (Weingrow, Fitch and Pigott 1941) to believe that this phenomenon of Sherrington might be localizable. Although this central excitatory state has been stressed in electroshock work on the human and in animals and has a place in the mechanism of the convulsion, its explanation along anatomic lines is far from simple. Even Rosett's implied bicellular theory alone will not suffice. There are too few collaterals for a convulsion.

Since the mammillothalamocortical tract and the final common pathway have been given detailed consideration as far as the physiology and anatomy are concerned, we shall see how what we have said in the foregoing applies to their relationship to the anatomical localization of the convulsion. As has been pointed out by Muskens, who referred to Stanly Cobb, it is indisputable that the tonic factor in a convulsion consists of a number of myoclonic reactions and that all of them can be interpreted on a neural bioelectric basis. It seems reasonable that since there might be a slow and fast component in a fit and the autonomic being related to the somatic reactions of a convulsion, that both the corticothalamomammillary system and the final common pathway might be the paths along which the convulsive reactions travel. Whether the continuous reaction of the tonic state is due to the paths of the bioelectric impulses in circular fashion along the internuncials of the above two systems, or that the fast and slow centripetal components are due to the fact that A, B, C, transmission variation rates along the two types of pathways are responsible, remains to be determined. Many writers like to include among the cells of the pyramidal system strands of autonomic fibres. Those who are fond of constructing theories will find a lot of food for thought in placing the motor as well as the autonomic components of a grand mal fit into this pathway. Such an idea would follow along the lines of Jackson and might satisfy all schools of thought that deal with centers. Whether the center is in the hypothalamus, midbrain, corpus callosum or cerebral cortex, the ubiquitous pyramidal system, with its widespread connections, might get there just the same. Such an arrangement would satisfy modern anatomically inclined epileptologists, particularly those of the Rosett school. At any rate, what has been said with regards to tonic and clonic mechanisms and their localization anatomically and physiologically heretofore, can be seen to apply with regards to the convulsive complex as succinctly stated in the following quotations from Pike, Notkin, Coombs and Weingrow (1933). "The first domain is that of localization, and practically every region of the central nervous system, has been included within it by one writer or another. The first attempt to put this part of the inquiry upon a definite anatomical basis, was that of Hughlings Jackson, who thought that convulsions, particu-

larly those of Jacksonian epilepsy, were due to some effect upon cells in the cerebral cortex. It will be recalled that, subsequent to his localization in the cerebral cortex of the cells of origin of the nervous impulses leading to the motor manifestation of convulsions, Jackson was led to postulate a theory of the evolution of the human nervous system and a further theory of the functional relation and organization of its various diseases in order to understand the varied phenomenon of convulsions. We have available today more facts drawn from a wider field of general biology than were available in Jackson's days, but the necessity of considering the problem of the convulsive disorders from the point of view of the functional organization and evolution of the nervous system is as pressing today as it was then. [Although we dislike interrupting the data by Pike, whose neurophysiologic work we greatly respect much more than our theoretical assumptions, we wish to remark upon Jackson since one of us (Weingrow) knows from personal contact with him how much there was experimentally in common between the thoughts of the two on the subjects of the mechanism of convulsions. The modern electroencephalographers seem to be imbued with Jackson's views of groups of cells going in unison into holocausts of discharges. They have picked up potentials of 500 to 2,000 microvolts from areas in which convulsions occur. They have followed Jackson's anatomical views and have picked up similar potentials electroencephalographically even when a convulsion is merely threatened. If they continue along such lines and eventually find a center which gives many times the above potential and is the cerebral vital node and bioelectric fountain (C. E. S.) remains to be seen.]" Compare the cortex and others in Fig. 55.

"Jackson broke sharply with tradition when he abandoned Kussmaul and Tenner's views that convulsions arose from a Krampfenzentrum in the medulla oblongata. (We shall elaborate extensively upon this since it involved chemical as well as physical views of outstanding authorities throughout a century up to the present.) The great viability of the hypothesis of convulsive centers in various regions of the nervous system makes it permissible to call attention to some of the conditions which such hypotheses must meet. It will be remembered that, in Jackson's own time, the objection was raised that unless the convulsion arose from the Krampfenzentrum in the medulla, it could not be considered true epilepsy. Any convulsive center in the medulla could act directly upon the cells of origin of efferent fibres in the medulla itself, and not upon cells of origin of fibres from any other region. It is doubtful whether the cells in the reticular formation give rise to a sufficient number of fibres to produce all the somatic and visceral responses of a typical convulsion in man or in the higher mammals, and no clonic convulsion is obtainable in higher mammals when all structures cephalad to the medulla are removed."

(In the foregoing pages we cited Muskens who mentioned Stanly Cobb's proof that a tonic contraction consists of a number of clonic ones. The proof was on a bioelectric basis. If the above is true it means that the volleys of bioelectric centrifugal impulses in a tonic contraction come so close together that muscular relaxation which is necessary for a clonic picture does not occur in the former.

Now that we are dealing with brain impulse manifestations of centripetal transmissions one begins to wonder about the role that centripetal plays as compared with centrifugal and projection transmissions of potential in general and as against association fibre transmissions in the production of crests and troughs of the normal electroencephalographic patterns.) "If disturbances arising in the medulla are supposed to excite fibres arising from cells higher up, one wonders just how such a center can act upon fibres with which it has no direct connections?" See brain stem theory Fig. 55.

"A similar argument could be adduced with reference to some other regions of the nervous system which have been held to be the site of origin of epileptic convulsions, and particularly those regions in which dead cells are found. No one has ever succeeded in getting a nervous impulse from a dead cell, and it is to the cells that are still alive that we must look for the origin of the nervous impulses which give rise to the motor phenomena of convulsions." (Mostly in the corticothalamomammillomesencephalic and in the Friedemann-Cajal loop sector system is it possible for one cell of the chain to be dead and yet enough to remain living so that the route of the convulsion could continue. Likewise, in the final common pathway, some cells of a system could be eliminated and a sufficient number could remain to transmit impulses to the internuncials below for the convulsion to take its course.) "The problem of localization and other aspects of epilepsy have recently been reviewed by Krause and Schumm, and we will not follow them further at this time."

The following data by Bing on convulsion centers and their significance will explain our audacious but enthusiastic interruption of quotations from the work of Pike. We realize how our enthusiasm has carried us away so that we embraced the anatomical viewpoint of a possible anatomical pathway responsible for convulsions. We know that Pike and his coworkers embracing the anatomical method differentiated between centers which carry the tonic and from those which carry the clonic features of the general convulsion. Muskens may have shared the same views but came out with the statement that the tonic is a combination of many clonic reactions. What the above statement means electroencephalographically is hard to say. Maybe deeper down in the brain there is a center (central excitatory state of Sherrington) that emits a unique potential pattern related to general convulsions. See Fig. 55 for the convulsive center theories.

Bing also commented upon the idea that there is an abundance of evidence for the existence of an epileptogenous center. According to Vogt, Frank, Pitres, Kussmaul, Sterling, Wimmer, Chartier and Schroeder, epilepsy not infrequently occurred in cases of diseases of the striatum, the thalamus and the medulla oblongata. According to Greving, Müller and Hoegner, generalized convulsion with loss of consciousness often occurred with sudden rise in blood pressure. The symptoms of the above would evidently involve parts of the corticothalamomammillary system. Authorities such as Barre, Draganesco, Lieou, Souques, Baruk and Bertrand found that an epileptogenous center might be located in the third ventricle because of the frequency with which convulsive attacks occur in association with tumors

in that region. Moreover, epilepsy was found as a frequent complication of pituitary tumors by Raymond, Souques, Laignel-Lavastine, Frankel, Fornairier, Loyd, Wolff and finally Chalk. The unusually high potentials obtained during convulsive episodes by modern bioelectrographers seems to point in the direction of the opinions of Pike, Sherrington and others who maintain that in the deeper cerebral(?) centers there are fountains of tonus. Whether these are linked with centers of tremendous potentials remains to be seen. It may be that some day some one will, by means of electroencephalographic leads, pick up this potential. In the above we are not theorizing, we are merely presenting views. Anyone interested in epilepsy cannot help but be fascinated by the progressive march of electroencephalography which has thus far followed almost every clinical manifestation of the fit with an electroencephalographic change in potential. It has been our experience (Fitch) that most often tumors in the above region of the third ventricle produce convulsive seizures only when penetration and infiltration occur into the anterior middle fossa or the infundibular region and finally affect the mammillary and other portions of the hypothalamus with which the corticothalamomammillomesencephalic and corticosupraopticomammillomesencephalic system as well as the final common pathway through the ansa lenticularis are connected. Further supporters of the above are other authors and among them Salmon, who claim that the epileptogenous zone is situated in the vicinity of the tuber cinereum and the infundibulum because of the rise of temperature, the somnolence, etc., which follow epileptic attacks. Against such comparisons between the quiescence of somnolence and that of the coma of the epileptic attack would be the fact that in the former the absence of consciousness is accompanied by a slowing of cerebration while in the latter there is no cerebration. A center that would, as in coma, slow up brain waves and hasten them as in convulsions and do it by the same cells has as yet not been proven to exist, i.e., the sleep center couldn't be one for consciousness.

From the foregoing it is evident that it is not improbable for the epileptic attack and its autonomic manifestation and particularly those which refer to the gastrointestinal and urinary system to follow along the same routes to which we have given so much time and space and to which we have referred so extensively from the literature, namely the corticothalamomammillomesencephalic and corticosupraopticomammillomesencephalic system as well as the motor and autonomic portions of the final common pathway. It seems that some of the authors presented above in relation to the epileptogenous center have, detoured, instead of favoring the pyramidal, stressed the extrapyramidal system that is the corpus striatum. This would be in agreement with the extensively elaborated and physiologically worked up detailed theory of Muskens. A lot more could be said in favor of the Musken's hypothesis, especially in regard to the thalamostriate and striothalamic relationships. We also feel about the above as we expressed ourselves about Watts and Fulton's views regarding the striothalamic relation with respect to neurogenic control of gastrointestinal function. It should be stressed that under the extrapyramidal we could include the cerebellum and its tegmental, vestibular, vestibu-

lotectal and other structures, stimulation of which produce vomiting, etc., etc. For the above refer to the convulsive striatal theory in Fig. 55.

From the above we can readily see how the neurophysiology of the convulsive mechanism falls in line with that of the physiology of the neurogenic control of gastrointestinal, urinary, water metabolism and possibly trophic vegetative functions. When our clinical material will be presented it will therefore be unnecessary to repeatedly refer to the above which has been extensively elaborated upon. From the above citation of the epileptic center schools the reader will see why we have, on so many occasions, concentrated upon Rosett and his work of simplification in relation to the anatomical explanation of the simplicity of the epileptic fit. Although he was an anatomist of great ability and one of the first to use hyperpnea in relation to convulsive tonus, his oversimplification of all mechanisms of tonus and motion seems to add confusion to many of the problems that face the student of epilepsy. What such a view confuses mostly is the operations of the autonomic in relation to the convulsive mechanism. It is too bad that this investigator, who made such an outstanding contribution to electroencephalography, did not give us an adequate explanation of that discovery and its implications. It will be up to the reader to realize that when we present our vegetative gastrointestinal syndromes in association with the type, frequency and other features of the convulsion that both the vegetative and somatic symptoms will be sufficiently backed by neurological findings as well as other procedures to substantiate the fact that the pathways under consideration and only such and their connections are involved. Without clinical proof functional concepts are often useless.

Continuing with the mechanism of the epileptic attack it may be noted that the physiology of the same involves not only the vegetative and motor features, but that chemical influences, not unrelated to sympathin and parasympathin, may be brought into play because of the autonomic physiology of the hypothalamus and other centers as they connect with the mammillothalamic and final common pathway. The epileptogenous center as stressed by Bing is an area which is very accessible to chemical and physical changes in the cerebrospinal fluid. Furthermore this area is well adapted to initiate generalized epileptic attacks because of its close anatomical connection with the subthalamus, the midbrain, and the medulla oblongata. Bing furthermore emphasizes that Demole, Marinesco, Horsley, Sager, Kreindler, Morgan and Gregory, and finally Cyon found that epileptic attacks have been induced experimentally through chemical or electrical stimulation of the infundibulum and the tuber cinereum or the hypophysis. The last mentioned author was not the only one nor were the preceding ones the only individuals who obtained convulsions by stimulation of the deep centers in the diencephalon and mesencephalon by direct stimulation. The number of workers along the above lines is legion and the interpretation of results exceeds that. The significant features in such experiments and their interpretations are the fact that some experimenters do not relinquish their hypotheses because a fact or two no matter how important seems to interfere with the general construction of their theories.

Muskens seems to have overthrown his anatomical concepts when he should have embraced Henry Head's(?) view that the cortex dissociates the tonic into clonic. See cortical theory in Fig. 55.

The reader can therefore be referred to an extensive field of investigation of most of our physiologic data dealing with the gastrointestinal, water metabolism, urinary, trophic and the convulsions, both chemical and electrical, as seen not only from the angle of structure and function in relation to the convulsive tonic and gastrointestinal tonic neurogenic control but also on a clinical basis. We have no space to elaborate further on this subject. It is interesting, however, to remark that the physiology of the same, that is the chemistry of sympathin and parasympathin which we have thus far failed to elaborate upon at length in relation to gastrointestinal tonus, might not be unrelated to the chemistry which is responsible for the induction of the convulsion. It will be interesting to note that adrenergic influences as well as those related to pituitrin and pilocarpine as enunciated by Cushing and various experimentalists when they applied the substances to the ventricles of the brain, all fall in line with such substances as absinthe and creatin as well as picrotoxin which also produce either a sympathetic or parasympathetic reaction but also are responsible for inducing and continuing the entire fit motor reaction in addition to the autonomic manifestation. It is common knowledge that such substances, while being related to metabolism in general and particularly to glucose and protein as well as amino acid metabolism, eventually all come down to the final chemical compound (F. C. C.) namely lactic and pyruvic acid. The work started by Berger and followed by Kornmuller, Lennox, Gibbs and Gibbs, Adrian, Mathews, and Dusser de Barenne will eventually solve the mystery of the mechanism of the convulsive state. Accompanying the electroencephalographic phases of this problem will be progress along biochemical lines in relation to the bioelectric. What role the autonomic will play in the rapid, almost daily accumulation of data will be seen. It will also be seen whether Musken's neurological data, both autonomic and otherwise, including gastrointestinal responses, will be stressed or lost in the avalanche of papers to come. Since in the presentation of our material the clinical data of which will fall along the anatomical avenues outlined above, it is not improper for us to add a little remark upon hyperpnea which is chemically and physically related to our anatomical structures, and is a method by which convulsions may be induced. Furthermore, we plan rarely in the cases to be presented to refer to, as we have done in our past publications, to the production of seizures by either hyperpnea or carotid sinus compression. Bing states that recently it has been found by electroencephalographic studies on an epileptic patient during hyperpnea that, in practically every case, wave patterns developed even though no convulsions occurred. This is of course present with every convulsion. There is much more than the above in the latest advances of the school of bioelectric epileptologists. The argument regarding the bioelectric basis of the convulsion, centers around the interpretation of the spike and cusp of focal epilepsy, as against the bilaterality of large voltage waves, in the "genetic" epilepsy of Lennox. It isn't therefore essential or hardly true any more to use the term idiopathic. The argu-

ment doesn't seem to have originated with the greatest investigator in the bioelectricity and biochemistry of epilepsy in this day, i.e., Lennox. The redeeming features of the electroencephalographic interpretations of the essential epilepsy curves is that they seem to point to the diencephalon and thus present an anatomical basis for their bilaterally synchronous potential. In this way the present school is right in siding with Jackson against Muskens. However, in their interpretations of spikes and cusps of focal epilepsy we see a bit of Muskens. From the last, it would seem that the spike is the result of interference with the normal curve in the same way as the Q. R. S. wave differs from the P and T waves in the electrocardiographs. Wherever present theories might lead, it may be noteworthy to stress, that from the writings of Brown-Sequard and the "Krampfenzentrum" advocates of the central sources of the convulsion, it seems that the last word has not been said on the mechanism of the convulsion, on its tonus and reflex background, on its neurology in attack pattern, and even on its sympathetic or parasympathetic components.

(To be continued)

BOOK REVIEWS

THE ART AND SCIENCE OF NUTRITION. Estelle H. Hawley, Ph.D. and Grace Carden, B.S. 700 pages, 91 illustrations, one in color. Third Edition. The C. V. Mosby Company, St. Louis, Mo., 1949. Price $4.75.

The book is divided into seven parts. The seventh is the appendix with many tables, etc. In going over this volume the reviewer finds many interesting and enlightening facts. However, his impression is that the general practitioner will not find time to read it, or may not value its contents. It is more likely that dieticians or those studying dietetics may find information which they may use to good advantage.

The review questions are worthwhile additions for the classroom.

FUNDAMENTALS OF OTOLARYNGOLOGY—A TEXTBOOK OF EAR, NOSE AND THROAT DISEASES. Lawrence R. Boies, M.D., Clinical Professor of Otolaryngology, Director of Division of Otolaryngology, University of Minnesota Medical School, and Associates. 443 pages, 184 figures. W. B. Saunders Company, Philadelphia, Pa., 1949. Price $6.50.

This book was written for the undergraduate student and the general practitioner. The text is clear and comprehensive and the illustrations are well done and explanatory.

"Dysphagia due to disorders of the esophagus" by Dr. Phelps is well illustrated and is recommended for reading by the gastroenterologist.

The chapter dealing with prescriptions and therapeutic procedures may be profitably read by all physicians.

For a ready reference volume it is a worthwhile addition to the book shelf.

A TEXTBOOK OF NEUROPATHOLOGY WITH CLINICAL, ANATOMICAL AND TECHNICAL SUPPLEMENTS. Ben W. Lichtensten, B.S., M.S., M.D., Associate Professor of Neurology, the University of Illinois College of Medicine, State Neuropathologist, Illinois Neuropsychiatric Institute. 1st Edition. 474 pages with 282 figures. W. B. Saunders Company, Philadelphia, Pa., 1949. Price $9.50.

Here is a book written by a specialist for undergraduate students and others interested in neurology and neuropathology.

The text is beautifully illustrated with gross and microscopic specimens found in pathological states of the nervous system. The description of these illustrations and the text dealing with the given subject is enlightening. General practitioners who are often confronted with patients presenting neurological symptoms will find useful information in these pages.

MODERN TRENDS IN DIAGNOSTIC RADIOLOGY. J. W. McLaren, M.A., M.R.C.S., M.D., Director, X-ray Department, St. Thomas Hospital, London, Examiner in Radiology, University of London. Illustrated. Paul B. Hoeber, Inc., New York, N. Y., 1948. 464 pages. Price $12.50.

This is another Hoeber book, which like the other volumes issued by this firm, is well printed, illustrated and indexed. It deals with general radiography of the entire body. Both the text and the explanations are instructive.

On page 427 the reader will find interesting information regarding blood changes in x-ray workers. It is advocated that the blood should be examined at intervals of not more than six months. A full blood count including an Arneth or Schilling index and sediment rate should complete the examination.

The reviewer recommends Diagnostic Radiology as a valuable addition to the already overcrowded shelf of the physician.

NERVOUS AND NEUROHUMORAL REGULATION OF INTESTINAL MOTILITY. W. B. Youmans, M.D., Professor of Physiology, University of Oregon Medical School. 129 pages. Interscience Publishers, Inc., New York, 1949. Price $4.75.

This volume is for the experimental laboratory rather than for the general practitioner or the specialist. Many interesting facts are brought out in these painstaking studies and experiments.

Chapter 14 describes the reflex effects on gastric and intestinal motility elicited by distention of the biliary system.

It is interesting to note that distention of the gallbladder may at times cause nausea and vomiting. Chapter 16 describes the hypothalamic and corticocerebral influences on gastrointestinal motility. A series of articles are currently appearing in The Review of Gastroenterology, dealing with this phase.

in peptic ulcer

He wants.....FAST RELIEF

You want.....FAST HEALING

Creamalin relieves ulcer pain in minutes because it is truly *amorphous* aluminum hydroxide, the form emphasized by Sollmann[1] as being most soluble. Greater solubility makes Creamalin rapidly available for neutralization. Also, Creamalin is a *reactive* gel. Reactive gels exhibit greater acid-combining power.[2]

Creamalin heals the lesion in 7 to 10 days because it is *acid-soluble* aluminum hydroxide, the nonabsorbable antacid which provides sustained neutralization at pH 4 to pH 5. Healing is fast because Creamalin inhibits pepsin activity and is "mucosal adherent." Tablets and liquid.

1. Sollmann, T.: A Manual of Pharmacology. Philadelphia, W. B. Saunders Co., 7th ed., 1948, p. 938.
2. Batterman, R. C., and Ehrenfeld, I.: Gastroenterology, 9:141, Aug., 1947.

Creamalin®

(AMORPHOUS ACID SOLUBLE ALUMINUM HYDROXIDE)

Winthrop-Stearns INC.

NEW YORK, N.Y. • WINDSOR, ONT.

The dress that needn't have been so beautiful

THERE'S NO REAL REASON for a girl to have the most beautiful dress in the world. Even my daughter Sally. Even if she has her heart set on it.

But—I bought it. And when I paid the bill, I whistled! Partly with the well-known father's bill-shock. Partly for happiness. Because, Sally was right—there never *was* a prettier dress to get married in.

It's times like that—when we can buy something really important even if it *is* a luxury—that I feel *lucky!*

I know the luckiest day of my life was when I signed up to save regularly through the Payroll Savings Plan at the office. I'd tried every which way to save before, but, brother, this *automatic* way is the only way that *works—for you—all the time!*

Buying U. S. Savings Bonds... whether by the Payroll Savings Plan or the Bond-A-Month Plan . . . is the safest, "foolproofest," easiest method of saving since money was invented. And every $3 you invest will turn into $4 in just 10 years.

Automatic saving is sure saving—
U.S. Savings Bonds

Contributed by this magazine in cooperation with the Magazine Publishers of America as a public service.

RELAX THAT SPASM with MESOPIN

When pain, heartburn, belching, nausea, or unstable colon are due to gastrointestinal spasm, Mesopin provides an effective means for prompt relief. Its selective antispasmodic action on the digestive tract controls spasticity without the undesirable side effects of atropine or belladonna. Thus, symptomatic relief of many common disturbances of the stomach or intestines can be achieved with discrimination and safety. Mesopin is indicated for the relief of gastrointestinal spasticity, such as pylorospasm, cardiospasm, spastic colon, and biliary spasm.

MESOPIN (brand of homatropine methyl bromide)

SELECTIVE GASTROINTESTINAL ANTISPASMODIC

SUPPLY: Elixir in 16 ounce bottles; tablets in bottles of 100.
MESOPIN (homatropine methyl bromide)—2.5 mg. per teaspoonful of elixir or per tablet. Also supplied: MESOPIN-PB*—2.5 mg. Mesopin and 15 mg. (1/4 gr.) phenobarbital per teaspoonful of elixir or per tablet.

Detailed literature and samples on request.

Endo®

*PB abbreviated designation for phenobarbital.

ENDO PRODUCTS INC., RICHMOND HILL 18, NEW YORK

"...about 50% of the patients who consult the general practitioner have complaints for which there is no discoverable physical or organic cause"[1]

Although these patients have no apparent organic basis for their complaints, they are ill and merit attention.

In functional disorders, response to stress is effected via both branches of the autonomic nervous system. Therefore, treatment consists, where possible, in removal of the emotogenic factor (practical psychotherapy) and the "partial blockade" of the efferent autonomic pathways. The family physician is well-qualified to help these patients; his advice will do much to achieve the desired change in habits and to avoid unhealthy situations.

Medical treatment is also essential. Controlled sedation of the entire autonomic nervous system can be accomplished by simultaneous administration of bellafoline (cholinergic inhibitor), ergotamine tartrate (adrenergic inhibitor) and phenobarbital (central sedative) in the form of Bellergal. This preparation inhibits autonomic impulses without completely blocking organ function.

Karnosh and Zucker[2] state that, "Probably the best medication for all neurovegetative disorders is a combination of: (a) bellafoline . . . (b) ergotamine tartrate ...(c) phenobarbital....A good commercial preparation of these ingredients is a tablet called bellergal . . . The adult dose of bellergal is 3 or 4 tablets daily."[3]

BIBLIOGRAPHY

1. WILLIAMS, V. P.: New England J. Med 236: 322, 1947.
2. KARNOSH, L. J. and ZUCKER, E. N.: A Handbook of Psychiatry, St. Louis, Mosby, 1945.

Sandoz Pharmaceuticals

DIVISION OF SANDOZ CHEMICAL WORKS, INC.
68 CHARLTON STREET, NEW YORK 14, NEW YORK

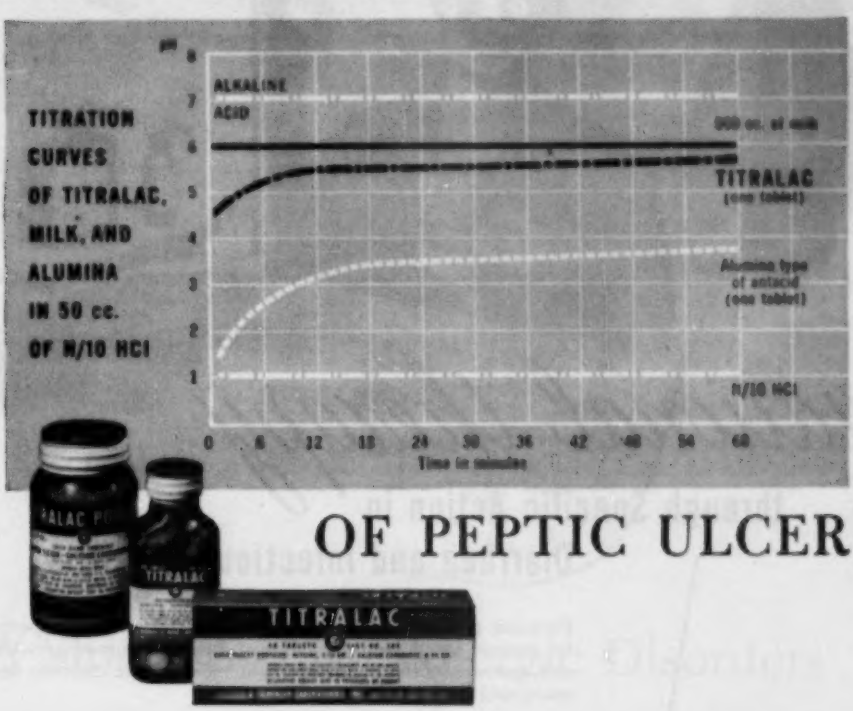
MANUFACTURERS OF
L. A. FORMULA
CONTAINING LACTOSE, DEXTROSE AND PLANTAGO OVATA CONCENTRATE

KONSYL produces normal intestinal activity . . . because it promotes peristalsis by adding bulk and lubrication to the intestinal contents. Non-habit forming, easy to take and well tolerated are other qualities which combine to make economical KONSYL the ideal medicament for patients who must "take something" every day.

Made from the jelly forming portion of Plantago Ovata, KONSYL absorbs and retains water, thereby aiding in the forming of soft, easily evacuated stools. It definitely will not interfere with normal digestive processes, nor will it cause leakage, irritation or flatuence. Send for a free professional sample and test its benefits in your own practice.

Burton, Parsons & Co. 1515 U STREET, N. W., WASHINGTON 9, D. C.

NON-SURGICAL TREATMENT



OF PEPTIC ULCER

Gastroenterologists have long endorsed the use of milk, when practicable, for its ideal acid-converting power and buffering capacity.[1, 2] In a recent comprehensive paper, Aaron[3] and others[4, 5, 6] express a preference for calcium carbonate as the antacid to be employed.

TITRALAC, by combining proper proportions of purified calcium carbonate and the amino acid glycine, *provides an acid-converting and buffering effect practically equivalent to that of fresh milk*, as shown in the above chart.* Just 1 TITRALAC tablet is equivalent to an 8-ounce glass of milk in antacid effect and provides quick and long-lasting relief from the distressing symptoms of hyperacidity.

The very agreeable taste of soft-massed TITRALAC tablets, which is achieved without employing taste-disguising, acid-generating sugars in the formula, makes them as acceptable to patients as an after-dinner mint. Prescribing TITRALAC eliminates the probability of unfavorable reactions often associated with the taking of metallic-tasting, astringent tablets or liquids, and ensures adherence to the prescribed dosage.

TITRALAC tablets are supplied in bottles of 100 and convenient-to-carry packages of 40. TITRALAC powder is also available, in 4-oz. jars.

REFERENCES

1. Rossett, N. E., and Flexner, J.: Ann. Int. Med. 18: 193 (1944). 2. Freezer, C. R. E.; Gibson, C. S., and Matthews, E.: Guy's Hosp. Reports 78: 191 (1928). 3. Aaron, A. H.; Lipp, W. F., and Milch, E.: J. A. M. A. 139: 514 (Feb. 19) 1949. 4. Kirsner, J. B., and Palmer, W. L.: Illinois M. J. 94: 357 (Dec.) 1948. 5. Kimball, S.: in Practice of Medicine (Tice). Hagerstown, Md., W. F. Prior Company, Inc., 1948, p. 210. 6. Special Article: M. Times 76: 10 (Jan.) 1948.

* The formula of TITRALAC is one whose composition and mode of action are recognized by U.S. Patent No. 2,429,366.

Samples and literature to physicians upon request.

SCHENLEY LABORATORIES, INC., 350 FIFTH AVENUE, NEW YORK 1, N. Y.

© Schenley Laboratories, Inc.

rational therapy

through Specific Action in Diarrhea and Infectious Enteritis

Paoguan presents sulfaguanidine, colloidal kaolin, and pectin for prompt action in many forms of infectious diarrhea, colitis, and gastroenteritis. Produces rapid relief of the diarrhea and associated abdominal discomfort.

Antibacterial The antibacterial action of sulfaguanidine is largely confined to the intestinal tract. It is but slightly absorbed, hence is remarkably free of toxic systemic reactions. It is the sulfonamide of choice in many forms of infectious enteritis.

Demulcent Pectin performs the valuable function of combining with certain toxins and exerting a well-defined demulcent influence upon inflamed intestinal mucous membranes.

Adsorbent Both kaolin and pectin are highly adsorptive and aid in the removal of toxins and bacteria, reducing the severity of the invasion.

Paoguan is available through all pharmacies in gallon and pint bottles.

THE S. E. MASSENGILL COMPANY
Bristol, Tenn.-Va.
NEW YORK • SAN FRANCISCO • KANSAS CITY

SEMCO

Each 5 cc. of Paoguan contains:

Sulfaguanidine	0.5 Gm.
Colloidal kaolin	2 Gm.
Pectin	0.04 Gm.

Combined in a palatable vehicle containing aromatics and carminatives.

PAOGUAN

SULFAGUANIDINE • PECTIN • KAOLIN

A Shield Against Allergic Disorders

DIATRIN* Hydrochloride

'WARNER'

A Superior Antihistaminic of Proved Value[1,2,3]

Effective · Less Toxic · Minimum Side-Effects

PACKAGE INFORMATION: Diatrin* Hydrochloride sugar-coated oral tablets, 50 mg each; bottles of 100 and 1000 tablets.

References

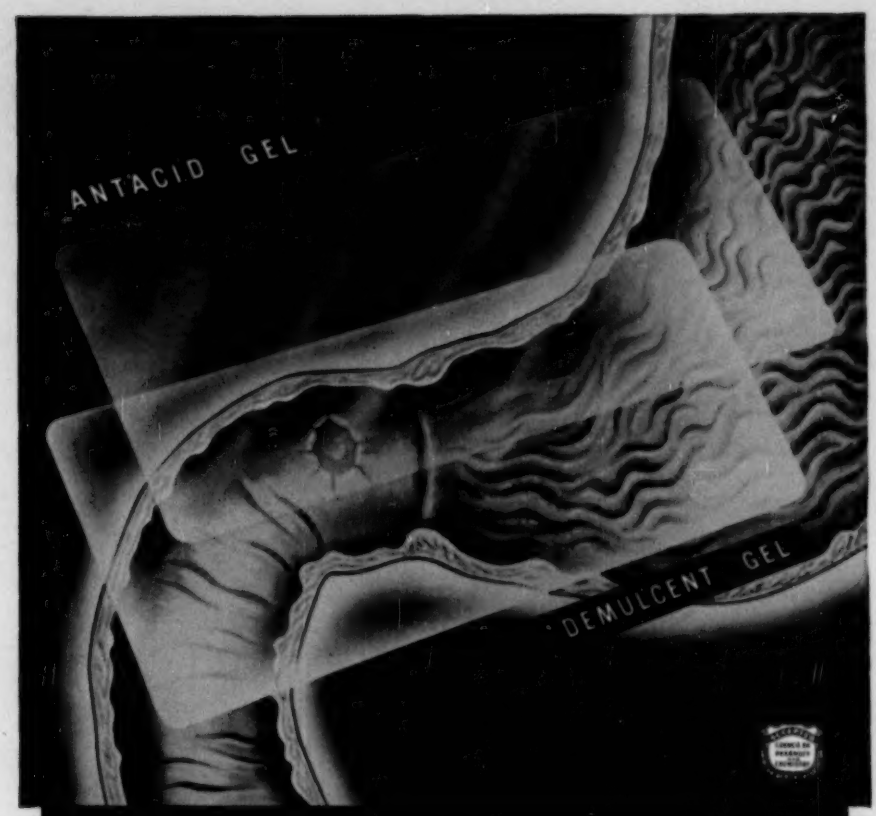
1. Combes, F. C., Zuckerman, R. and Canizares, O: Diatrin Hydrochloride; A New Antihistaminic Agent for the Treatment of Pruritus and Allergic Dermatoses, *Ann. of Allergy*, 7:676, 1949.

2. Kugelmass, I. N.: Antihistaminic Therapy of Allergic Disorders in Infants and Children, *N. Y. State J. M.*, 49:2313, 1949.

3. Combes, F. C., Zuckerman, R. and Canizares, O.: Diatrin Hydrochloride; Clinical and Toxicologic Studies of a New Antihistaminic Agent, *J. Invest. Dermatol.*, 13:139, 1949.

*T. M. Reg. U. S. Pat. Off.

WILLIAM R. WARNER & CO., INC. New York, St. Louis



Double gel action

AMPHOJEL

ALUMINUM HYDROXIDE GEL
ALUMINA GEL

Wyeth

Double protection for the peptic ulcer patient
Amphojel, the unique "two-gels-in-one" product, provides:

- chemical protection by reacting with gastric acid to reduce acidity to noncorrosive levels; and
- physical protection because its demulcent gel content acts like a "mineral mucin," which favors the natural healing process.

Bottles of 12 fl. oz. at all drugstores.

Wyeth Incorporated, Philadelphia 3, Pa.